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Evidence for improving services for glaucoma in Nigeria

Epidemiology, ophthalmologists' practice pattern, patients' access to care and community experiences of glaucoma

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Declaration

I, Fatima Kyari, confirm that the work presented in this thesis is my own. Where data and information have been derived from other sources, I confirm that these have been indicated in the thesis.

One of the three components of this thesis was analysing data from the Nigeria national blindness and visual impairment survey. I played an important role in the design of the questionnaire and data collection for this survey, as I examined half the survey participants i.e. approximately 7,000 adults in 150 sites across the country. I also had responsibility as team manager for ensuring the quality of the survey, including the data collected. I play an important role in writing up the survey findings for publication (16 papers to date).

For my PhD, I went back to the original findings, and reviewed and interpreted all the visual field data, classifying those where there was field loss suggestive of glaucoma. I also devised a diagnostic algorithm, based on international criteria, which uses three ocular parameters and three levels of evidence to identify participants with glaucoma. Once I had identified participants with glaucoma I was able to analyse the data for part of this thesis.

All analyses were undertaken by me, with advisory support from my supervisor and an epidemiologist.

FKyari

Signature Dated 10th September 2016

Abstract

Glaucoma is the second leading cause of blindness worldwide. Africa region has the highest burden of glaucoma and glaucoma blindness. When diagnosed early and appropriate treatment sustained, blindness from glaucoma is avoidable.

The Nigeria national blindness and visual impairment survey (NBS), with >13,500 people aged $\geq$40 years examined, estimated the prevalence of blindness as 4.2% (95%CI 3.8-4.6%). 16.7% was due to glaucoma, the leading cause of irreversible blindness and functional low vision. There are insufficient population-based glaucoma studies in Africa; and the NBS provided the largest dataset in Africa from which data on glaucoma could be derived.

In this study, analysis of the NBS data using established criteria from the International Society of Geographical and Epidemiological Ophthalmology showed high prevalence of glaucoma (5.02%; 95%CI 4.60-5.47%): undiagnosed in 94%; and open-angle glaucoma (OAG) in 86%. One-in-five persons with glaucoma were blind. Increasing age and higher intraocular pressure were independent risk factors for OAG; and some ethnic groups were more at risk. Glaucoma blindness was associated with socioeconomic deprivation, reflecting poor access to care. These findings underscored the high level of need for optimal glaucoma services.

Information about glaucoma management obtained from 153 practising ophthalmologists in Nigeria highlighted patient-related challenges of late presentation with advanced disease and poor compliance to treatment; and additional constraints due to inadequate access to equipment for diagnosis and treatment.

In the qualitative study, we sought to understand access to glaucoma care and determine why people with glaucoma are presenting late for treatment. We found barriers of access to care which could be explained as evidence of structural inequalities associated with coping mechanisms and distinct social suffering.

This study provided data required to develop evidence-based strategy for control of glaucoma blindness by improving glaucoma services in Nigeria. These data could also have implications to other Sub-Saharan African countries with similar socioeconomic and ecological characteristics.

Format of the Thesis

The thesis for this PhD uses the ‘research/reviews papers’ format. It therefore includes a number of different but related journal articles which have either been published in, accepted by, or are formatted for submission to peer-reviewed journals. The chapters listed in italics in the Contents are in this research/review paper format and include publication details in a cover sheet, including acknowledgement of the contributions of other people. The other chapters of the thesis are composed of ‘linking material’, which includes information/data not covered in the papers and helps to make the thesis a coherent body. The linking material was written by Fatima Kyari.

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In the name of God, the most Gracious, the most Merciful.

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My friends have been gracious; in particular, TO and UY have helped me to be accountable towards achieving my objectives and ensured that I stayed focused. I appreciate the beautiful times I shared with my friends, especially with ZSB together with our children.

My superb family are my pillar of strength and they gave me the most. I would not have accomplished this work without their support and they have my deepest gratitude and love.

Dedication

The work presented herein is dedicated to my two properly lovely and amazing children Halima Dahirey and Zayyan; that they may prosper and soar higher, by His Grace.

Contributors to the research presented in this thesis

Person	Position	Contribution
Clare Gilbert	Professor of International Eye Health, LSHTM	PhD supervisor and Principal Investigator for the NBS
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Winifred Nolan	Moorfields Eye Hospital NHS Foundation Trust	PhD advisory committee
Paul Spry	University Hospitals Bristol NHS Foundation Trust	PhD advisory committee
Clare Chandler	Medical anthropologist, LSHTM	PhD advisory committee and advice on qualitative study design and analytical support
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LSHTM = London School of Hygiene and Tropical Medicine; NBS = Nigeria national blindness and visual impairment survey; NHS = National Health Service; CEO = chief executive officer; CBM = Christoffel Blindmission; CBRO = community-based rehabilitation officer.

Chapter 1

Glaucoma clinical care and community perception

Participants in the community departing from a clinical examination site

Introductory material about glaucoma classification, clinical care, knowledge and awareness of glaucoma

1.1 Definition and classification of glaucoma

Glaucoma, in the public health context, is an optic neuropathy associated with characteristic structural damage to the optic nerve and associated visual dysfunction.[1] These are seen clinically as enlargement of the optic disc cup and loss of field of vision. Glaucoma can be classified according to anterior chamber angle morphology into open-angle glaucoma (OAG) or angle-closure glaucoma (ACG).

The diagnosis of glaucoma in prevalence surveys has been standardised and is based on the following three levels of evidence, according to the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) definitions of glaucoma.[1]

Level 1 evidence entails having a cup:disc ratio (CDR) $\geq$97.5th percentile or CDR asymmetry $\geq$97.5th percentile and characteristic visual field defect detected on the threshold pattern deviation plot; or on the suprathreshold screening result where threshold testing was indicated but not done.

Level 2 evidence is where there are no visual field test results and the CDR or CDR asymmetry is $\geq$99.5th percentile. Included at this level of evidence is expert opinion adjudication if there is relative afferent papillary defect (RAPD) or raised intra-ocular pressure (IOP).

Level 3 diagnosis is made where the disc cannot be visualised for CDR assessment but the visual acuity (VA) is <3/60 in the better eye and the IOP $\geq$99.5th of normal or there is evidence of filtration surgery. Expert opinion adjudication is also included at level 3 diagnosis.

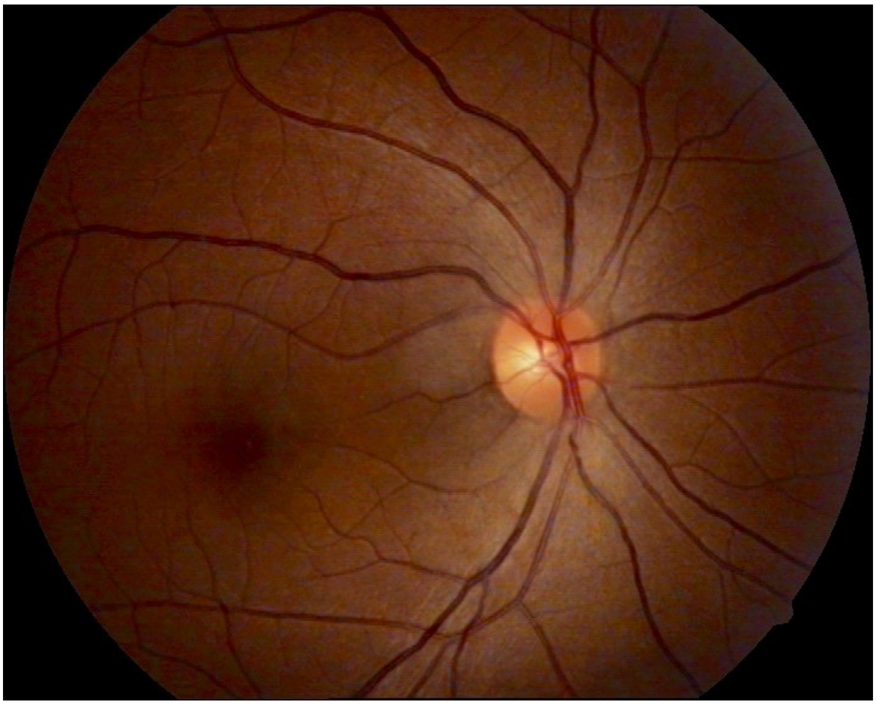

Figure 1a: Optic disc with a normal cup:disc ratio

Figure 1b: Glaucomatous optic disc

1.2 Clinical presentation and risk factors for glaucoma

Glaucoma causes irreversible blindness due to loss of ganglion cells of the optic nerve. There have been a few hospital-based studies[2-6] that have helped to define pattern of glaucoma morbidity and risk factors for glaucoma in Nigeria. In an analysis of patients presenting to the hospital with glaucoma in south-western Nigeria 22% were blind, 15% had ACG and 10% were younger than 30 years old. The persons with ACG were more likely to present at a younger age, have worse visual acuities, more visual field defects and higher IOP.[3] Similarly, in northern Nigeria, 12.5% of glaucoma patients were 30 years old or younger.[2] The proportion of glaucoma patients presenting with blindness was up to 42% in these studies.[2-5] Older patients living further away from the hospital were more likely to present with more advanced/end-stage disease.[6] Other socio-demographic risk factors associated with blindness and late presentation included lower socio-economic class, being less educated and earning lower monthly income.[7] Other factors associated with glaucoma were positive family history, increasing IOP, CDR greater than 0.7 and diabetes mellitus.[8] Increasing age was the most consistent factor associated with glaucoma.

Generally, possible risk factors associated with glaucoma[9-14] are:

1. Related to socio-demographic attributes:
    a. Increasing age
    b. Ethnicity – of African origin
    c. Male sex
    d. Positive family history
    e. Occupation – lower income cadres
    f. Rural residence
2. Features associated with incipient disease:
    a. Larger CDR
    b. Retinal nerve fibre layer (RNFL) atrophy
    c. Disc haemorrhage
    d. Peri-papillary atrophy (PPA)
3. Ocular morphology/anatomical features:
    a. High refractive error (myopia or hyperopia)
    b. Increased diameter of the optic nerve head

    c. Thinner central corneal thickness (CCT)

4. Intra-ocular pressure (IOP)
5. Pseudoexfoliation syndrome
6. Related to vascular functions and systemic conditions
    a. High blood pressure
    b. Diabetes mellitus
    c. Sickle-cell disease
    d. Reduced ocular perfusion pressure (Blood pressure minus IOP)
    e. Increasing body mass index (BMI)
7. Drugs:
    a. Corticosteroids
8. Other factors
    a. Infrequent or no previous eye exam
    b. Late diagnosis
    c. Non-compliance with therapy

1.3 Visual fields assessment and Frequency Doubling Technology (FDT) perimetry

To make the diagnosis of glaucoma, structural abnormalities of the optic disc need to be supported by evidence of functional abnormality, principally visual field defects. There is a need for early detection of visual field loss because structural alteration in the disc and nerve fibre layer precedes functional abnormality.[15] There are many different methods and instruments that can be used to detect visual field abnormalities, the “gold standard” being standard automated perimetry (SAP).

Another instrument uses Frequency Doubling Technology (FDT) and it has been shown to have high sensitivity and specificity in the detection of early glaucomatous functional loss.[16] FDT machines are compact, portable and a quick method for visual field testing. The FDT provides rapid screening in 45 to 60 seconds and full-threshold testing in 4 to 5 minutes. It has been demonstrated to have reasonable sensitivity and specificity in detecting eye disease[17] and high specificity for detecting glaucomatous visual field damage.[18, 19] The threshold C20 test provides a higher sensitivity than the screening suprathreshold C20-1 strategy.[20] Clinical validation studies of the FDT using the Humphrey Field Analyzer (HFA) 24-2 SITA suggest that threshold testing using the FDT is comparable with the HFA 24-2 SITA-fast test pattern.[21]

Figure 1c: Visual field testing with the FDT machine

1.4 Clinical management of glaucoma

Studying glaucoma in populations has increased the understanding of the fundamental nature of the disease and various clinical trials have informed the clinical diagnosis and treatment of glaucoma.[22-26]

According to recommendation of the UK's National Institute for health and Clinical Excellence (NICE) guidelines,[27] the diagnosis of glaucoma in clinical settings would include slit lamp Goldmann applanation tonometry, pachymetry to measure central corneal thickness, gonioscopy to assess anterior chamber angle features, perimetry using the standard and central threshold test for visual fields and optic nerve head assessment with dilatation, using stereo slit-lamp biomicroscopy with a condensing lens (Hruby lens or +60, +78, +90 Dioptres). The diagnostic protocol outlined is similar to that recommended by the International Council of Ophthalmology (ICO)[28] and the American Academy of Ophthalmology (AAO).[29, 30] ICO recommends additional documentation of optic disc morphology with colour stereo-photography or computer-based image analysis.

According to the NICE guidelines, the treatment recommended as first-line is a prostaglandin analogue, or a beta-blocker in moderately elevated IOP. Surgery with anti-metabolites are reserved for those at risk of vision loss despite medical treatment.

Reduction in IOP is the only treatment shown to be effective in glaucoma.[23, 24, 26, 31] Interventions to prevent blindness from glaucoma aim at lowering IOP to prevent deterioration of vision; and include surgical (mostly filtration procedures), laser and medical therapies. Early diagnosis and commencement of treatment is an important factor in prevention of blindness from glaucoma. A study of the natural history of OAG in the Early Manifest Glaucoma Trial (EMGT) showed that many of the untreated patients progressed slowly and the median rate of progression from a full field to blindness was 70 years.[32] However, a substantial minority progressed rapidly with median rate of progression to blindness in 25 years. The United Kingdom Glaucoma Treatment Study (UKGTS), a randomised, triple-masked, placebo-controlled trial, has demonstrated visual field preservation with the IOP-lowering prostaglandin analogue eye drops (latanoprost 0.005%).[33] Latanoprost is the most commonly used anti-glaucoma medication in developed countries.

While highlighting acceptable surgical outcomes for trabeculectomy in Nigeria,[34-38] the difficulties and challenges in diagnosis and treatment of glaucoma in West Africa due to limited equipment, lack of treatment options, high cost of medications and lack of awareness of patients have been elucidated.[39-44] However, recommendations for diagnosis and management of glaucoma in West

Africa lack evidence, as there has not been much operational research or clinical trials to determine the best option for glaucoma management in Nigeria. Patients with glaucoma often present very late to eye care facilities, and lack of awareness and the cost of treatment are likely explanations.[3-7]

1.5 Cost of glaucoma treatment

With better understanding of the disease, newer medication for treatment and new diagnostic technology increase the cost of management. Anecdotal reports indicate that in a resource-limited environment, a systematic approach is required for management decisions and to improve treatment outcomes. Prostaglandin analogues are being recommended as first-line drugs because of their IOP lowering efficacy and safety profile. Based on this and other new medications, the cost of glaucoma treatment was found to have increased by 227% in the Republic of Ireland.[45] There is also an increasing linear trend in direct cost as disease severity worsened,[46] such that managing glaucoma and delaying the progression would reduce the economic burden of the disease. In real out-of-pocket terms, Egyptian patients with glaucoma spent, on average, 30% of their monthly income on glaucoma medications,[47] and Nigerian patients spent at least 50% of their monthly income on glaucoma medications.[48] On the long-term, this is not affordable and it poses great economic challenges on the patients thereby leading to non-compliance of treatment.

Figure 1d: A selection of glaucoma medicines available in Nigeria (2012)

1.6 Public awareness and knowledge of glaucoma

There is an increasing body of evidence that shows that in Africa there is limited awareness of glaucoma among patients and communities. For example, in a study in Nigeria of hospital patients with glaucoma, only 18% had heard of the disease before their diagnosis though 94% believed it to be a serious condition.[49] In Tanzania, patients did not understand the cause and chronicity of the disease.[50] Likewise, among an urban population in India[51] and Ghana[52] there was low level of awareness of glaucoma. Higher levels of education, increasing age, being female and positive family history of glaucoma were determinants of awareness.[51]

Unlike cataract, glaucoma did not have a local name in most of the communities studied. Ophthalmologists were the key source of information about glaucoma for 80% of patients studied in an Egyptian hospital.[47] Forty per cent did not know that glaucoma could cause blindness. Even among Singapore Chinese patients suffering from acute angle closure, glaucoma awareness was low (22.9%).[53] Lack of awareness was associated with increasing age, lack of formal education and unemployment. Indeed, the gradual effects of glaucoma on vision enabled many patients to cope with the diminishing visual ability before their diagnosis and they had assumed these were part of normal life.[54] Many of these studies underscore the importance of providing information to enhance the understanding of glaucoma especially to those at risk. This may facilitate earlier clinical presentation and better acceptance of treatment.

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Chapter 2

Epidemiology of Glaucoma in Sub-Saharan Africa: Prevalence, Incidence and Risk Factors

Sunset at the Bakana creeks of the River Niger delta

Review paper containing literature review of published data about prevalence, incidence and risk factors of glaucoma in Sub-Saharan Africa

(*Appendix 6: Journal editorial commentary – Strengthening institutional capacity for glaucoma care in Sub-Saharan Africa*)

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Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Middle East African Journal of Ophthalmology (MEAJO)		
When was the work published?	April-June 2013		
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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conceived the title of the review paper. I did the literature search. I wrote the first draft and prepared the subsequent revisions with consideration of comments from co-authors.

Student Signature: Kyari **Date:** 28 June 2016

Supervisor Signature: CGilbert **Date:** 30 June 2016

Epidemiology of Glaucoma in Sub-Saharan Africa: Prevalence, Incidence and Risk Factors

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ABSTRACT

Purpose: The purpose of this study is to review the epidemiology of different types of glaucoma relevant to Sub-Saharan Africa (SSA) and to discuss the evidence regarding the risk factors for onset and progression of glaucoma, including risk factors for glaucoma blindness.
Methods: Electronic databases (PubMed, MedLine, African Journals Online- AJOL) were searched using the full text, Medical Subject Headings (MeSH) terms, author(s) and title to identify publications since 1982 in the following areas: population-based glaucoma prevalence and incidence studies in SSA and in African-derived black populations outside Africa; population-based prevalence and incidence of blindness and visual impairment studies in SSA including rapid assessment methods, which elucidate the glaucoma-specific blindness prevalence; studies of risk factors for glaucoma; and publications that discussed public health approaches for the control of glaucoma in Africa.
Results: Studies highlighted that glaucoma in SSA is a public health problem and predominantly open-angle glaucoma. It is the second-leading cause of blindness, has a high prevalence, an early onset and progresses more rapidly than in Caucasians. These factors are further compounded by poor awareness and low knowledge about glaucoma even by persons affected by the condition.
Conclusion: Glaucoma care needs to be given high priority in Vision 2020 programs in Africa. Many questions remain unanswered and there is a need for further research in glaucoma in SSA in all aspects especially epidemiology and clinical care and outcomes involving randomized controlled trials. Genetic and genome-wide association studies may aid identification of high-risk groups. Social sciences and qualitative studies, health economics and health systems research will also enhance public health approaches for the prevention of blindness due to glaucoma.

Key words: Africa, Epidemiology, Glaucoma prevalence, Glaucoma risk factors, Open-angle glaucoma, Sub-Saharan Africa

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INTRODUCTION

Data from population-based surveys (PBS) indicate that glaucoma is the second leading cause of blindness, accounting for 8% of blindness among the 39 million people who are blind world-wide.[1] In Africa, glaucoma accounts for 15% of blindness and it is the region with the highest prevalence of blindness relative to other regions world-wide[2] (Adapted from Resnikoff, 2004)[2] [Table 1]. In 2006, the number of individuals estimated to be bilaterally blind from glaucoma was projected to increase from 8.4 million in 2010 to 11.1 million by 2020.[3] However, the numbers who are blind is just the tip of the iceberg as there are many more individuals with glaucoma who are at risk of blindness. In 2006, modeling the available data, it was estimated that 60.5 million

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Table 1: Blindness prevalence and glaucoma-specific blindness prevalence by WHO sub-regions

WHO sub-region[,]	Blindness prevalence estimate. All ages (%)	Proportion of blindness due to glaucoma (%)	Glaucoma-specific blindness prevalence	
			All ages (per 1000)	Age 40+ years (%)
Afr-D	1.00	15	1.50	0.8
Afr-E	1.00	15	1.50	0.8
Sear-B	1.00	14	1.40	0.8
Emr-D	0.97	11	1.07	0.6
Emr-B	0.80	10	0.80	0.4
Eur-C	0.40	20	0.80	0.4
Wpr-B1	0.60	11	0.66	0.4
Eur-B1	0.40	15	0.60	0.3
Sear-D	0.60	9	0.54	0.3
Wpr-A	0.30	18	0.54	0.3
Eur-B2	0.30	16	0.48	0.3
Wpr-B2	0.80	6	0.48	0.3
Amr-B	0.30	15	0.45	0.3
Amr-D	0.50	8	0.40	0.2
Amr-A	0.20	18	0.36	0.2
Eur-A	0.20	18	0.36	0.2
Wpr-B3	0.30	6	0.18	0.1
World	0.57	12.3	0.70	0.4

[α]Afr: WHO African Region, Amr: WHO American Region, Emr: WHO Eastern Mediterranean Region, Eur: WHO European Region, Sear: WHO South-East Asian Region, Wpr: WHO Western Pacific Region, [β]A=Mortality stratum 0.1%, B or C = mortality stratum 0.15%, D or E = mortality stratum 0.2%, WHO: World Health Organization

people world-wide would have glaucoma by 2010, increasing by 20 million by 2020. The Africa region also has the highest incidence and prevalence of glaucoma[3] (Adapted from Quigley, 2006)[3] [Figure 1]. The prevalence of glaucoma is similar among the Caucasian populations of Europe,[4] USA[5,6] and Australia[7,8] being less than the prevalence in Latinos in the USA[9] and people of Asian origin.[10-17] The black populations of the Caribbean,[18,19] Africa[20-23] and USA[5] have the highest prevalence of open-angle glaucoma (OAG).[24-26] Furthermore, there appear to be differences in the prevalence of glaucoma in different black populations in the Caribbean islands and within Africa,[24] which may be attributed to genetic diversity as well as environmental and socio-economic factors.[27,28]

Who goes blind from glaucoma is influenced by the age of onset of glaucoma and the natural history[29] as well as access to services,[30-33] the quality of care provided[34] and adherence to treatment and follow-up.[32,33] There is some evidence that glaucoma has an earlier age of onset in blacks[5,35] and has a more aggressive clinical course.[34,36,37] In Africa, there are the additional factors of poor awareness,[38-45] poor access to care, and less than optimal diagnosis and management.[46-53] Socio-economic deprivation exacerbates the situation, leading to very late presentation.[54-59] Indeed, in Africa, glaucoma has been referred to as the "silent thief of sight."[60]

Lately, there has been increased momentum about glaucoma care in Africa. At the World Glaucoma Association 1st Africa glaucoma summit in Ghana in 2010, a decision was made to strengthen and incorporate glaucoma management, training and education into existing programs.[61] The Kampala resolution in 2012 called upon all those involved in glaucoma management "to highlight the importance of controlling vision loss from glaucoma as an integral part of eye healthcare and in health and safety policies."[62]

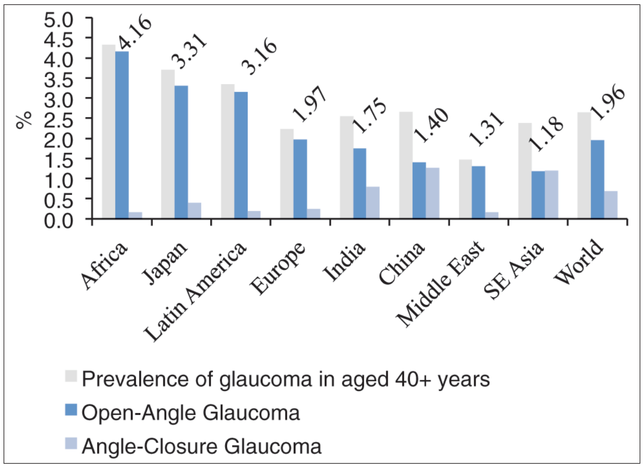

Figure 1: Prevalence of glaucoma in population aged 40+ years (%) in 2010 by World Health Organization sub-regions (Labeled figures indicate percentage values for prevalence of primary open angle glaucoma)

The purpose of this review is to describe the epidemiology of the different types of glaucoma in Sub-Saharan Africa (SSA). The scope of the review encompasses published data on the prevalence and incidence of glaucoma and discusses the evidence regarding risk factors for the onset and progression of glaucoma, including risk factors for glaucoma blindness. The designation SSA refers to the geographical area of Africa that lies south of the Sahara desert including Sudan and comprises 48 countries[63] and this review also included studies of other black populations outside SSA.

Studying glaucoma in populations has public health implications as it allows identification of potential risk factors for the disease as well as the blinding consequences, enabling control strategies to be targeted to groups most at risk. These, together with clinical intervention studies, inform diagnostic and therapeutic approaches that can be applied to patients with glaucoma, hence contributing to the Kampala resolutions.

DEFINITIONS

Glaucoma is an optic neuropathy associated with characteristic structural damage to the optic nerve and associated visual dysfunction,[64] which are seen clinically as enlargement of the optic disc cup and loss of field of vision. It is classified according to the anterior chamber angle morphology into OAG or angle-closure glaucoma (ACG). The morphological classification is very important because the types have different characteristics and present in varying proportions in different populations. OAG and ACG have different natural histories and risk factors and require different management strategies,hence the importance of gonioscopy in the classification of glaucoma. A further classification is by etiology into primary or secondary glaucoma.

A standard definition and classification system for glaucoma was proposed in 1998 by the International Society of Geographical and Epidemiological Ophthalmology (ISGEO)[64] principally for use in population-based prevalence. The definition considers glaucoma as a group of diseases defined by end-organ (optic nerve) structural damage and functional deficit. In the ISGEO classification, glaucoma is defined by three levels of evidence, regardless of angle morphology (from Foster, 2000)[64] [Table 2]. The highest level of evidence is when both structural damage and functional deficit are seen; that is a large vertical cup:disc ratio (VCDR) and/or asymmetry between the two eyes. A large disc is defined by the distribution of cup:disc ratios in the normal population, an abnormally large disc being defined when it is ≥97.5th percentile of the VCDRs of the normal population. The 1st level evidence also requires characteristic defects in the visual fields (VF). The 2nd level requires greater structural damage of the optic disc (i.e., VCDR ≥ 99.5th percentile, or asymmetry) when VF testing is not possible. The 3rd level is where VCDRs cannot be assessed and VF testing is not possible and the diagnosis of glaucoma is based on other clinical parameters: most importantly, intraocular pressure (IOP), visual acuity of less than 3/60 on the Snellen's chart and medical history (e.g., previous glaucoma surgery).

METHODS

Search methods

Electronic databases (PubMed, Medline, African Journals Online- AJOL) were searched using the full text, Medical Subject Headings (MeSH) terms, author(s) and title to identify the relevant publications. The search terms used were glaucoma, prevalence (in title), Africa (and names of each of the countries) open-angle, angle-closure, blindness, and visual impairment. The search was restricted to publications in the last three decades (from 1982 to 2012) and papers and/or abstracts available in English. The following publications were included: (1) population-based glaucoma prevalence surveys in SSA; (2) population-based glaucoma prevalence surveys or incidence studies in African-derived black populations living outside Africa; (3) population-based prevalence surveys and/or incidence studies of blindness and visual impairment studies in SSA, including rapid assessment methods, which elucidate the cause-specific blindness prevalence due to glaucoma; (4) PBS in SSA and African-derived black populations, which reported risk factors for glaucoma and/or glaucoma blindness; and (5) publications that discussed public health approaches for the control of glaucoma in Africa. Reference lists of cited articles were searched for additional publications not identified by the database searches.

PBS of blindness and visual impairment and rapid assessment of avoidable blindness (RAAB) surveys that did not have data on the proportion of visual impairment or blindness due to glaucoma were excluded. Hospital/facility-based studies were not included.

Strengthening the reporting of observational studies in epidemiology (STROBE) guidelines

Population-based glaucoma prevalence surveys in SSA and black populations living outside Africa were critically appraised using the STROBE guidelines.[65,66] These guidelines are to assess the clarity of reporting in relation to completeness and accuracy, but are not designed to assess the quality of the research. The completeness and accuracy of the reports aided the interpretation and the generalizability of the results. The 22 key points enumerated on the STROBE checklist for cross-sectional studies were assigned one score each. Some of the key points appraised included: "presenting key elements of study design early in the paper; describing the setting, locations, and relevant

Table 2: ISGEO definition for glaucoma in prevalence surveys

Level of evidence for the diagnosis of glaucoma	Parameter			VA	Medical history
	VCDR	VF	IOP		
Level 1	≥97.5th %	Typical defect			
Level 2	≥99.5th %	Not available			
Level 3	Not available	Not available	≥99.5th %	<3/60	e.g., Surgery for glaucoma

ISGEO: International society of geographical and epidemiological ophthalmology, VCDR: Vertical cup:disc ratio, VF: Visual fields, IOP: Intraocular pressure, VA: Visual acuity dates, including periods of recruitment, exposure, follow-up, and data collection; mentioning the eligibility criteria, and the sources and methods of selection of participants; clarity on diagnostic criteria; describing all statistical methods, including those used to control for confounding; reporting numbers of individuals at each stage of the study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed; reporting other analyses carried out." A numerical summary score was given to each of the publications and an arbitrary classification was applied. Papers that scored >75% were classified as good, those that scored 55-75% were classified as satisfactory and those that scored <55% were classified as incomplete.

RESULTS

Search results summary

PBS of glaucoma in SSA

A total of nine studies[20-23,67-71] were identified and all were included [Table 3]. Using the STROBE guidelines,[65,66] three were classified as good,[20-22] one was satisfactory[67] and five had incomplete reporting.[23,68-71]

PBS of glaucoma in African-derived populations living outside Africa

Four glaucoma prevalence studies[5,18,19,72] [Table 3] and one glaucoma incidence study[73] were included in the review. Using the STROBE guidelines, three surveys were classified as good.[5,18,19]

PBS of prevalence/incidence of blindness and visual impairment in SSA

Fifty-five publications were identified. Of these, 32 prevalence surveys[74-105] [Table 4] and the only incidence study identified[106] were included in this review. Glaucoma was not clearly defined and/or was not mentioned as a specific cause of blindness in the other PBS of prevalence and RAAB publications.[107-128]

Population-based studies that reported risk factors for glaucoma in SSA and African-derived populations

One report on risk for incident open-angle glaucoma[129] and 10 further publications that discuss risk factors for glaucoma were included in this review.[130-139]

Prevalence of glaucoma

There are few PBS data that provide prevalence estimates of any/all types of glaucoma in SSA[20-23,67-69] [Table 3], and only four provided reliable estimates.[20-22,67] Of these, three were undertaken in different districts in South Africa[21,22,67] and one in the Kongwa region of Tanzania.[20]

The surveys in Kongwa, Tanzania,[20] Hlabisa, South Africa[21] and Temba, South Africa[22] conducted the study on people aged 40 years and above; had robust methodologies, with a well-described sampling strategy, and detailed descriptions of IOP measurement and VF assessment. Gonioscopy and optic disc examination methods were clearly described. Two of the surveys[21,22] were analyzed using the ISGEO classification [64] and IOP was included as a diagnostic criterion only when optic discs could not be assessed and VFs were not obtainable. The prevalence estimates of all types of glaucoma were 4.5% (95% confidence interval [CI] 3.2–6.1%) and 5.3% (CI 3.9-7.1%) respectively. The other study in Mamre, South Africa[67] also studied those aged 40 years and above. The prevalence estimate was similar (4.6%; CI not reported) but the methodology was less rigorous. The survey in Kongwa, Tanzania[20] used three diagnostic criteria based on the optic disc and VF definitions. When definite field defects in association with compatible disc changes were used to define glaucoma, the prevalence of all types of glaucoma was 4.16% (CI 3.5-4.9%).

The other studies used different methods and had limitations, which may have affected the estimate of glaucoma. For example, a survey in south-eastern Nigeria[69] used IOP as a major diagnostic criterion and disc assessment was performed by direct ophthalmoscopy through an undilated pupil. In this survey, the prevalence of glaucoma was 2.1% (CI not reported) in people 30 years and older. In northern Nigeria,[68] a survey of individuals aged 5 years and above reported the prevalence of glaucoma to be only 0.55% (CI 0.07-1.99%) in the 361 participants examined aged 35 years and above; and 1.02% (CI 0.12-3.64%) in the 196 participants aged 45 years and older. Glaucoma was defined based on typical glaucomatous disc appearance or IOP greater than 30 mmHg if the disc was not visualized. A further survey in southern Ghana,[23] which used European glaucoma study guidelines, did not use stringent diagnostic criteria, and those with media opacities with no view of the disc were excluded. Another limitation was the sampling strategy, which was largely a volunteer sample and included family members of those with a positive family history of glaucoma. In this survey, the prevalence of OAG was 8.4% (CI 7.74-9.06%) in those 30 years and older, which is likely to be an over estimate. A study reported from western Cameroon,[71] which also used a voluntary sample, reported the prevalence of glaucoma to be 8.2% (CI not reported). Another study in Nigeria[70] excluded persons with IOP greater than 21 mmHg and did not assess VFs. In this survey, the prevalence of glaucoma suspects was 2.7% (CI not given). Previous authors suggested in 2009 that a conservative estimate of the prevalence of glaucoma in Africa in people 40 years and older be 4%.[46]

There have been four glaucoma surveys among black populations living outside Africa [Table 3]. In the Caribbean region, the prevalence of glaucoma in African-Caribbeans was 8.8% (CI not given) in those aged 30 years and above in St Lucia[18] and 6.8% (CI 6.1-7.6%) in aged 40 years and above in Barbados.[19] In African-Americans in Baltimore, USA[5] the glaucoma prevalence

Table 3: Population-based surveys of glaucoma by types and racial origin

Racial origin/Ethnic group	Year	Location of study	Age (years)	Examined/Sample size (Response rate %)	Prevalence of glaucoma§				Un-diagnosed glaucoma (%)	Proportion blind# (%)	Clarity of reporting using STROBE checklist∞	Reference
					All glaucoma (%)	POAG (%)	PACG (%)	Other forms of glaucoma (%)				
African												
Bantu (Wagogo)	2000	Kongwa, Tanzania	40+	3247/3641 (89.2)	4.16	3.10	0.59	0.49	98.5	14.1	Good	[20]
Bantu (Zulu)	2002	Hlabisa, South Africa	40+	1005/1115 (90.1)	4.50	2.70	0.10	1.70	90.2		Good	[21]*
Bantu (Sotho and Nguni)	2003	Temba, South Africa	40+	839/1120 (74.9)	5.30	2.90	0.50	2.00	87.1 (of POAG)	41 (of eyes with POAG)	Good	[22]*
SE Asian and W European	1993	Mamre, South Africa	40+	987/1194 (82.7)	4.66	1.52	2.33	0.81 (angle recession)	78.3	33 (of POAG)	Satisfactory	[67]
Hausa-Fulani	2001	Kaduna, Nigeria	35+ 45+	361/430 (83.9) 196/239 (82.0)	0.55 1.02	0.55 1.02	-	-	-	15.2	Incomplete	[68]
Ibo	2002	Enugu, Nigeria	30+ 40+	664/946 (70.0)	2.10 2.78	-	-	-	85.7	-	Incomplete	[69]
Akwapim, Ewe, Akim, Ga-Adangbe	2004	Akwapim-South, Ghana	30+ 40+	1785/1843 (96.9)	7.7§ 8.5§	8.40	0.50	-	93.0	-	Incomplete	[23]
Ekpeye (Igbo extraction)	2009	Rivers, Nigeria	All ages	866/960 (89.0)	2.7 (glaucoma suspects)	-	-	-	-	9.5	Incomplete	[70]
Bamileke; Bamum	2009	Western Cameroon	5 to 90	635/-	-	8.20	-	-	-	-	Incomplete	[71]
African-derived												
African-Caribbean	1989	St. Lucia	30+	1679	8.8	-	-	-	-		Good	[18]
African-American	1991	Baltimore	40+	5308/5023 (94.6)	-	Blacks 4.74§ Whites 1.29§	-	-	About half	5.3 (of POAG)	Good	[5]
African-Caribbean; mixed	1994	Barbados	40+	4709/5640 (83.5)	-	All 7.1§ Blacks and mixed 6.8§ Whites 0.8	-	0.7	51.0	-	Good	[19]
African-Caribbean	1994	London	35+	873/-	3.9	-	-	-	58.0	0	Incomplete	[72]

§Adjusted rates if reported, #Proportion of glaucoma participants that are blind, ∞Outcome of appraisal by adequately including STROBE key points: >75%-good, 55-75% satisfactory, <55% incomplete *Survey conducted according to ISGEO criteria for glaucoma definition, ISGEO: International society of geographical and epidemiological ophthalmology, POAG: Primary open angle glaucoma, PACG: Primary angle-closure glaucoma, STROBE: Strengthening the reporting of observational studies in epidemiology

Table 4: Glaucoma cause-specific blindness prevalence and proportion of blindness due to glaucoma as percentage of total blindness in SSA

Location/Country of study	Year	Age (years)	Examined Sample	Blindness prevalence, all causes (%)	Proportion of blindness due to glaucoma (%)	Ranking of blindness due to glaucoma	Glaucoma blindness prevalence in study population (%)	Glaucoma blindness prevalence in 40+ year olds	Reference
South Africa	2003	40+	839	5.60	32.0	2	1.79	1.79	[22]
Cameroon	2007	40+	2215	4.10	29.0	1	1.19	1.19	[74]
South Africa	2002	40+	1005	3.20	22.0	2	0.90	0.90	[14]
Nigeria, national	2009	40+	13,599	4.20	16.7	2	0.70	0.70	[75]ø
Ethiopia	2003	40+	2693	7.90	7.7	3	0.61	0.61	[76]
Ghana	2005	40+	2298	2.80	20.6	2	0.58	0.58	[77]ø
Ghana	2012	40+	5603	1.20	21.7	3	0.26	0.26	[78]ø
Eritrea	2011	50+	3163	9.00	15.2	2	1.37	0.80	[79]
Liberia	2012	50+	3,544	4.10	16.0	2	0.66	0.38	[80]
Malawi	2011	50+	3430	3.30	15.8	2	0.52	0.30	[81]
Nigeria	2006	60+	445	5.60	42.0	2	2.35	0.70	[82]
Nigeria	2005	30+	480	10.40	6.0	4	0.62	1.02	[83]
Equitorial Guinea	2002	All	3218	3.20	13.3	4	0.43	2.36	[84]
Nigeria	2007	8 to 92	2201	1.20	33.3	2	0.40	1.54	[85]
Nigeria	2003	All	1964	1.22	20.8	3	0.25	0.25	[86]
South Africa	1993	All	6090	1.00	22.9	2	0.23	1.27	[87]
Ethiopia	1995	All	60,820	1.10	17.0	4	0.19	1.04	[88]
Nigeria	2004	All	-	1.18	15.8	3	0.19	1.04	[89]
Malawi	1986	6+	1574	1.27	-	3	0.19	0.90	[90]
Nigeria	2007	All	1248	1.10	14.3	2	0.16	0.87	[91]
Uganda	2002	13+	4076	0.40	38.5	1	0.15	0.53	[92]
Cameroon	1996	All	10,647	1.20	12.0	2	0.14	0.80	[93]
Mali	1996	All	5871	1.70	8.1	3	0.14	0.77	[94]
Cape Verde	2006	All	3374	0.80	15.4	2	0.12	0.68	[95]
Nigeria	1996	All	2921	0.90	11.1	3	0.10	0.56	[96]
Benin	1995	All	7047	0.60	15.0	2	0.09	0.50	[97]
Ethiopia	1997	All	7423	0.85	9.5	3	0.08	0.45	[98]
Kenya	1990	All	13,803	0.70	-	3	0.06	0.33	[99]
Central African Republic	1997	All	6086	2.20	2.2	4	0.05	0.27	[100]
Togo	1989	All	11,081	0.82	6.0	3	0.05	0.27	[101]
Gambia	2000	5+	13,046	0.42	9.0	3	0.04	0.18	[102]ø
South Africa	1988	All	18,962	0.57	6.0	4	0.03	0.19	[103]
Congo	1990	All	7041	0.30	9.0	2	0.03	0.15	[104]
Gambia	1989	All	8174	0.70	2.0	-	0.01	0.08	[105]

40+ year-olds as 18% of the total population, 50+ year-olds as 10.5% of the total population, øVisual field examination done, SSA: Sub-Saharan Africa

in those aged 40 years and above was 4.74% (CI 3.81-5.67%) among blacks, being four times higher than in whites (1.29%, CI 0.80-1.78). A prevalence of 3.9% (CI not given) was reported in a cross-sectional study of a voluntary sample of African and Caribbean people aged 35 years and above living in London.[72]

The prevalence of glaucoma in the studied populations aged 40 years and older in the Tanzania[20] and South Africa[21,22,67] surveys (range 4.2% to 5.3%) was comparable to the 4.2% prevalence in the African-American population of Baltimore,[5] but much lower than the prevalence of 7.1% in the African-Caribbean population of Barbados.[19] Although these surveys were not completely comparable as the definitions of glaucoma varied and the methodology was not uniform, a consistent pattern was revealed: that glaucoma is a public health problem in SSA.

Types of glaucoma

Where glaucoma was classified by angle morphology, OAG was approximately six times more prevalent than ACG in SSA[20-23] [Table 3]. The exception was a study in those of mixed South-East Asian and western European origin in Mamre, South Africa.[67] In this study, Salmon reported a prevalence of 2.3% for ACG and 1.5% for OAG. However, 12 participants (1.2%) had full VFs and were classified as having ACG on the basis of their angle configuration only, without evidence of functional deficit. If the ISGEO definition of functional visual deficit had been used the prevalence estimate for ACG would have been lower. Nonetheless, the findings indicate that in SSA, ACG is more prevalent in those of SE Asian origin than in blacks. Pseudoexfoliation, aphakic glaucoma, uveitic glaucoma, lens-induced, and post-traumatic angle-recession glaucoma were classified as secondary glaucoma,[20-22,67] with the prevalence ranging from 0.49% in Kongwa, Tanzania[20] to 2.0% in Temba, South Africa.[22] Exfoliative glaucoma was responsible for 16% of all glaucoma in Temba[22] and 21.6% of all glaucoma in Hlabisa in South Africa,[21] but was not detected in Kongwa, Tanzania.[20]

The publications for the surveys in the African-derived populations living outside Africa were reports for OAG and did not give prevalence of other types of glaucoma except in Barbados where the prevalence of secondary glaucoma was 0.7%.[19]

Incidence of glaucoma

Incidence rates provide evidence of long-term risk of a disease and are important for planning services and for policy. The cumulative incidence is the number of new cases seen over the time of observation divided by the population at risk. There are no PBS that report observed incidence of glaucoma in SSA. In the African-descent population of Barbados, the 9-year incidence of definite OAG was 4.4% (CI 3.7-5.2%) or 0.5%/year and showed an increased risk with age and in men.[73]

Awareness of glaucoma

A total of nine surveys reported whether or not participants with glaucoma knew they had the disease or if they were receiving treatment [Table 3]. In Kongwa, Tanzania,[20] 98.5% did not know they had the disease. Similarly, 90.2% in Hlabisa, South Africa[21] and 87.1% (of those with Primary OAG) in Temba, South Africa[22] were not aware they had the disease. In Mamre, South Africa,[67] 36 (78.3%) were newly diagnosed and another six out of the seven participants that were blind due to glaucoma were already receiving treatment. Ninety-three per cent in Akwapim-South[23] and 85.7% in Enugu, Nigeria[69] were newly diagnosed. Approximately, half in both racial groups (blacks and whites) in Baltimore[5] as well as in Barbados[19] did not know they had the disease.

Glaucoma blindness

Incidence of glaucoma blindness

In Uganda, the all-cause incidence of blindness was 9.9/1000 person years, with glaucoma accounting for 3.6% of incident cases (i.e., 0.36/1000 person years).[106] In the Barbados eye studies, OAG was the 2nd leading cause of incident blindness, accounting for 14.3% of the 9-year incidence (1%) i.e., 0.143% over 9 years.[140]

Proportion of people with glaucoma who are blind

The only SSA glaucoma prevalence surveys, which reported the proportion of participants with glaucoma who were blind were those conducted in Tanzania, South Africa and Ghana. The proportions were as follows: 14.1% in Kongwa, Tanzania,[20] 33% (of OAG) in Temba, South Africa,[22] 15.2% in Mamre, South Africa,[67] and 9.5% in Akwapim-south, Ghana.[23] In the Temba survey, 58% (32 of 55) of those with any type glaucoma were blind in at least one eye.[22] In Hlabisa, South Africa study, 41% of eyes with OAG were blind.[21]

In the Baltimore eye survey, the proportion of participants with OAG who were blind was 5.3%.[5,141]

Glaucoma-specific blindness prevalence

Data on the glaucoma cause-specific blindness prevalence were available from the following sources: PBS of blindness and visual impairment, RAAB studies and World Health Organization (WHO) published data.

From the available data, the glaucoma-specific blindness prevalence was calculated for those aged ≥40 years, assumed to be 18% of the total population [Table 4]. In the seven surveys in which the studied populations were aged 40 years and older,[21,22,74-78] the glaucoma-specific blindness prevalence ranged from 0.26% in Ghana[78] to 1.79% in Temba, South Africa.[22] In the recent RAAB studies conducted in Eritrea,[79] Liberia[80] and Malawi,[81] the glaucoma blindness prevalence in the study population of 50-year olds and above were 1.37%, 0.66% and 0.52%, respectively. Glaucoma was the second or leading cause of blindness[74,92] in the more recent surveys, but ranked third of fourth in older surveys, after cataract and corneal diseases. However, in all the surveys included in this review, only six had VF assessment as part of the examination protocol.[75,77,78,102,109,126] In all the other surveys, glaucoma was diagnosed only as a cause of blindness and only included those who had lost central fixation in both eyes.

In Hlabisa, South Africa, the prevalence of blindness was 3.2% (CI 2.2-4.6%) in people aged 40 years and above, and 22% was due to glaucoma.[21] In Temba, South Africa, the prevalence of blindness was 5.6% (CI 3.9-7.7%) in people 40 years and older and the proportion due to glaucoma was 32%.[22]

A recent nationally representative population based survey of blindness and visual impairment in Nigeria reported the all-cause prevalence of blindness to be 4.2% (CI 3.8-4.6%)[142] and the proportion of blindness due to glaucoma was 16.7% among those aged ≥40 years.[75] The prevalence of blindness ranged from 3.3% (CI 2.4-4.5%) in the Delta ecological zone to 6.6% (CI 4.2-10.4%) in the northern Sahel ecological zone, and the proportion of blindness due to glaucoma varied from 13.2% in the Sudan Savannah to 23.5% in the Sahel ecological zones. The nationwide overall glaucoma-specific blindness prevalence was 0.7% (CI 0.55-0.88%)[75] with a four-fold difference in the glaucoma-specific blindness prevalence which ranged from 0.4% (CI 0.2-0.9) in the Delta to 1.6% (CI 0.6-3.8%) in the Sahel.[143] A high prevalence of blindness in all ages was reported in Bioko, Equatorial Guinea (3.2%)[84] and this was reflected as high prevalence estimate of glaucoma blindness of 2.36% in the 40+ year-olds. A high prevalence of blindness (10.4% in people

30 years and older) was reported in a survey in leprosy villages in north-eastern Nigeria, where glaucoma ranked 4th as a cause of blindness, nevertheless, with a high glaucoma-specific blindness prevalence of 1.02% in the 40+ year-olds.[83] This is in contrast to a survey undertaken decades ago in an area endemic for onchocerciasis in North-Eastern Nigeria where the prevalence of blindness was 11.8% in all ages and glaucoma did not feature as a cause as almost all blindness was due to onchocerciasis.[128]

In the Baltimore eye survey,[141] the overall prevalence of blindness was 1.21% and the proportion of blindness due to glaucoma was 14.1% among those aged 40 years and above. The glaucoma-specific blindness prevalence was 0.17%. Glaucoma blindness was compared between whites and blacks. In the blacks, glaucoma blindness was 0.37% and 6.6 times higher than the 0.06% glaucoma blindness prevalence in whites. Glaucoma blindness also occurred earlier in blacks with a prevalence of 0.29% in the age-group 50-59 years whereas none of the whites were blind due to glaucoma before the age of 60 years. In this population, glaucoma as well as cataract and diabetic retinopathy were more common as a cause of visual impairment in blacks while macular degeneration was more so in whites.[144]

Data on the prevalence and causes of blindness were published by WHO for the year 2002.[2] Survey data available at the time were extrapolated to countries without data in order to derive global estimates. The glaucoma-specific blindness prevalence was calculated from these data, which are presented according to the 17 WHO sub-regions [Table 1]. The proportion of blindness in all ages due to glaucoma globally was 0.7/1000, ranging from 0.18/1000 in the Western Pacific sub-region B3 to 1.5/1000 in both African sub-regions. Glaucoma blindness in Africa is, therefore, twice the global figure; and eight times higher than in the Western Pacific sub-region.

Risk factors

The study of risk factors gives information on who gets glaucoma (incidence studies), who has glaucoma (prevalence studies), who progresses and who goes blind due to glaucoma (risk of progression, prognostic factors). Risk factors for glaucoma incidence were reported from the Barbados eye study.[129] Risk factors for glaucoma prevalence were reported in six of the PBS of glaucoma in SSA[20-23,67,69] and in all four of the PBS of glaucoma in the African-derived populations.[5,18,19,72] Ten other publications related to the Akwapim-South, Ghana survey,[139] St Lucia survey,[137] Barbados eye study,[130] Baltimore eye survey,[132,133,135,136] African descent and glaucoma evaluation study,[134] a multicenter study[138] and a PBS in African-Americans living in Canada[131] reported risk factors for glaucoma.

Who is at risk of developing glaucoma?

Risk factors for incident OAG were increasing age, higher IOP, lower systolic blood pressure (BP) to IOP ratio (BP/IOP), lower mean diastolic ocular perfusion pressure (diastolic BP minus IOP), thinner central corneal thickness (CCT), and a positive family history.[129] Racial variability of some of these risk factors at baseline has been demonstrated;[130] with higher IOP[131] and thinner CCT[131,134] in African-derived groups.

Who has glaucoma?

Age was an important and consistent risk factor, with a higher prevalence of glaucoma associated with increasing age.[5,19-23,69,72,130] The age-specific prevalence of OAG was higher with increasing age: From 1.7% (CI 1.1-2.5%) to 5.6% (CI 3.1-9.2) in Kongwa, Tanzania,[20] from 1.2% (no CI reported) to 4.9% in Hlabisa, South Africa,[21] and from 0.6% (no CI reported) to 6.0% in Temba, South Africa,[22] in the age-group 40-49 years and the age-group 70-79 years, respectively. Similarly, higher prevalence of OAG was reported from 1.4% (CI 0.8-2.2%) to 14.8% (CI 12.5-17.4%) in Barbados;[19] and from 1.23% (CI 0.23-2.24%) to 9.15% (CI 5.83-12.48%) in blacks and from 0.92% (CI 0.2-7.2%) to 2.89% (CI 1.44-4.34%) in whites in the Baltimore eye survey,[5] in the age-groups 40-49 years and 70-79 years, respectively.

Gender was not consistently associated with prevalent cases of glaucoma.[5,23,69] However, some surveys reported a higher prevalence of OAG in men.[19,21,22,67,130] Men were also more likely to have secondary glaucoma,[22] especially following trauma.[67] ACG was more common in women.[67]

Higher IOP is another important factor associated with a higher prevalence of glaucoma,[20,21,130,132] although IOP had a limited predictive value.[21] Hypertension was not significantly associated with glaucoma prevalence.[20,72,130] However, lower mean ocular perfusion pressure was associated with a higher prevalence in the surveys in African-derived populations of Barbados[130] and Baltimore[135] but, this was not reported in African-Caribbeans in London[72] or in the only survey that this factor was studied in SSA.[20] These factors associated with ocular blood flow i.e., systolic BP, diastolic BP and ocular perfusion pressure were stronger in older people.[132,133,135]

A positive family history of glaucoma was associated with higher prevalence of glaucoma.[130,133]

The higher prevalence of glaucoma in blacks compared to whites was consistently demonstrated in the surveys involving the two racial groups.[5,19,72] Furthermore, those with darker skin and of African birth seemed to have a higher risk.[72] However, in the two studies involving a number of ethnic groups in SSA, ethnicity was not associated with a variation in prevalence of glaucoma;[22,23] but the sample sizes were relatively small and the studies were confined to limited geographical areas with few ethnic groups represented.

Other risk factors for glaucoma include lower body mass index in men and history of cataract surgery.[130]

Who has glaucoma progression and who develops blindness due to glaucoma?

A survey in Ghana[139] explored the risk factors associated with severe disease and surveys in Baltimore[132] and St Lucia[137] explored the risk factors for glaucoma progression and blindness. The Temba, South Africa survey[22] was the only SSA survey that described the age of participants that were blind due to glaucoma. The risk of glaucoma blindness increased with increasing age. The average age of the blind glaucoma participants was higher (74.8 years) when compared to the average age (65.4 years) of the non-blind participants. In the Ghana study that combined population-based and facility-based samples, older age (more than 60 years) and IOP greater than 31 mmHg were associated with more severe disease and the absence of family history was associated with delay in seeking treatment.[139] Increasing age was also associated with progression of the disease.[136,137] Aggressive glaucoma therapy reduces the progression of VF loss that leads to bilateral blindness;[136] and the proportion of patients with progressive VF loss is much higher in those untreated than in treated eyes.[137] Glaucoma progression was more severe in blacks[138] and blindness occurred at an earlier age in blacks than in whites.[141]

DISCUSSION

World estimates on the prevalence of glaucoma and glaucoma blindness prevalence have been derived from projections and modeling from pooled data and surveys,[3] and by extrapolating data from countries with data to those without,[2] and more recently, using newly developed imputation methods based on country economic status.[1] However, these approaches have given different estimates for glaucoma. One explanation for the WHO estimates of glaucoma blindness being lower than other estimates is that data were obtained from population based surveys of blindness, where VF are usually not included in the definition of blindness. Individuals with extensive VF loss, but with preserved central fixation in at least one eye would not, therefore, be included in the WHO estimates. Another reason may be that age-standardization is included in modeling estimates and this will take into account the steep decline in population after age 40 years that is typical of developing country profile.

The number of high quality glaucoma surveys conducted in Africa is low and it is difficult to extrapolate the findings to wider populations as they were conducted in limited and defined geographical areas of large countries. These surveys were also often not directly comparable due to variation in the age of participants, and differences in the methods used to measure parameters of relevance to glaucoma and to define and classify the disease. Only two surveys used the ISGEO definition, which relates IOP and cup:disc ratios to population norms. This is important, given the recognized variation in the distribution of optic disc and cup size and IOP between populations.[12-16,64,145-149] There is only one small study of the incidence of glaucoma blindness in Africa,[106] and no studies on the incidence of glaucoma. Longitudinal studies to address these questions will also give information on the natural history of the disease, as a high proportion of individuals diagnosed with glaucoma do not seek treatment even when this is recommended.

More reliable data are required from large scale, rigorous PBS in order to revise and refine the prevalence and magnitude estimates of glaucoma and glaucoma blindness for SSA. Ideally, the surveys should use the same age range, and the standard definitions and classification system, and use comparable methods of assessing VF, IOP and cup:disc ratios. The sample sizes should be large enough to allow analysis of risk factors for glaucoma in order to identify the population most at risk. Ideally, such surveys should also collect data on family history of glaucoma and socio-demographic data. Data on whether different ethnic groups in SSA are more at risk than others is currently lacking, as there are no published studies, which have included a large enough sample of different ethnic groups. The relatively small sample size of the reviewed surveys would limit the power of the studies to detect differences. Data from the Nigeria national survey[150] are currently being analyzed and will provide data on risk factors including variations in ethnic groups. Again, this information would be of value for targeting control strategies.

The suggested prevalence of glaucoma in SSA of 4% in people 40 years and older[46] is a reasonable estimate as that is what these three "good" studies in SSA indicated.[20-22] Since, this prevalence estimate was suggested in 2009 for Vision 2020 planning purposes, there has been no additional high quality data to suggest that it needs to be changed.

The available evidence suggests that the prevalence of glaucoma is higher in SSA and in people of African descent who live outside Africa. A Bayesian meta-analysis that examined the relationship between OAG prevalence and age, gender, and racial group also showed that the pooled random effects prevalence of OAG was higher in the black populations (4.2%).[26] Given the lack of evidence that environmental and behavioral risk factors are associated with glaucoma, these findings suggest a genetic basis for the greater susceptibility in blacks.[28] The genetic basis of glaucoma is being increasingly recognised[151,152] and genetic research and genome-wide association studies in Africa will possibly explain some of the variations and excess risk seen in black populations.

The most prevalent type of glaucoma in SSA is open-angle glaucoma. However, hospital-based studies tend to overestimate the proportion of ACG reporting a range of 6% to 18% of all glaucoma cases seen;[54,153-157] and this may be related to the health-seeking behavior in which the pain in acute ACG acts as a trigger for the need to obtain treatment.

The very low awareness of having the disease as reported in the PBS signifies that only a small fraction of people with glaucoma access healthcare, leaving a large majority untreated and with the potential blinding effects. Indeed, in those that access healthcare, up to 42% of glaucoma patients presented with advanced disease and bilateral blindness; and over half were blind in one eye.[54-59]

Glaucoma causes irreversible blindness due to loss of ganglion cells of the optic nerve leading to vision and VF loss. The proportion of people with glaucoma who are blind is higher in SSA than in any other region. The earlier age of onset of the disease in blacks has already been reported[35] and this has been corroborated in the PBS in SSA[20-22] and black populations where the prevalence of OAG in the age-group 40-49 years was much higher than in white populations of USA and Barbados.[5,19] Interestingly, a similar variation of the 40-49 years age-specific prevalence of 0.4% (CI 0.0-0.9%) and 3.1% (CI 0.4-5.8%) between the white and non-white groups, respectively, in Piraquara City, Brazil was reported.[158] Comparatively, the 40-49 years age-specific prevalence in Caucasian Australians was 0.2% (CI 0.0– 0.56%),[8] and remarkably from as low as <0.2% (no CI reported)[159] and up to 1.5% (CI 0.4-2.5%)[160] in indigenous Australians. Glaucoma progression is also more aggressive in blacks.[36,37,138] Thus one of the plausible reasons why blacks in Africa and African-derived populations have more glaucoma blindness is that the early age of onset means they have the disease for a longer time.

The Nigeria national survey on blindness and visual impairment is the largest PBS that has ever been carried out in Africa. The prevalence data by geo-ecological zones showed wide variation between the Sahel and the Delta ecological zones. The proportion of blindness due to glaucoma was also higher, with a 4-fold difference in the prevalence of glaucoma blindness.[143] The only explanations are that the incidence of glaucoma blindness is higher and/or the disease is more aggressive and/or access to care is lower in the Sahel zone. Data on these factors are currently being analyzed.

Further studies are needed to explore risk factors for glaucoma blindness, which will help to identify those most at risk for example by gender, socio-economic status (e.g., level of education), age, and ethnic group. Exploration of biomedical risk factors associated with disease progression (e.g., IOP and ocular perfusion pressure) will also provide guidelines for setting and monitoring target IOP following treatment.

The ranking of glaucoma as a major cause of blindness from lower ranks in older surveys to second leading cause in most recent surveys may be attributable to the increase in control efforts of corneal diseases, notably vitamin A deficiency and trachoma which became less in magnitude, and a decrease in onchocerciasis blindness. In addition, the classification and diagnosis of glaucoma had improved in more recent surveys. However, it is probable that figures for glaucoma prevalence and blindness are underestimations especially in populations with a high prevalence of cataracts. Cataract and corneal diseases are more easily diagnosed in surveys and may occlude the view of the optic disc for a definite diagnosis of glaucoma. Furthermore, in ranking of principal cause of blindness using the WHO format, cataract or corneal scar may take precedence being recorded preventable causes of blindness even in eyes with co-existing glaucoma.

A large number of the PBS from which data of glaucoma-specific blindness prevalence were derived did not have VF assessments. These data therefore underestimate glaucoma-specific blindness which, if using the WHO definition of blindness, should also include those with a central VF of less than 10 degrees in the better eye.[161] The wide variation in glaucoma-specific blindness prevalence may be attributable to the sampling methodology and/or some studies done in areas where focal diseases were more prevalent. In addition, the definitions used for blindness as well as for glaucoma and the age of participants in the surveys varied. The age of the sample is very important since the disease is age-related. Even if definitions and measurements were standardized and the sample populations were all 40+ years, there could still be very different prevalence data because of the differences in the life expectancy and age structure of people aged 40 years and above between populations and regions. Age-standardization between the surveys would have eliminated the differences due to confounding by differences in age structure of the populations.

A limitation of this review process is that age-standardization of these data was not possible. Another limitation is that there was a language restriction in the search strategy. If a publication and abstract were not in English they might have been missed. However, this would only apply to Francophone and Lusophone Africa.

Application of these studies to the control of glaucoma in SSA

These studies have highlighted that glaucoma is predominantly OAG and it is a public health problem in SSA. It has a high prevalence, an early onset and progresses more rapidly than in Caucasians; and it is a major cause of blindness. Thus case-finding strategies need to be targeted at younger ages. Treatment needs to be more aggressive, life-long and with adequate follow-up, and monitoring of patient-physician contact frequency.

Challenges for the control of glaucoma in African populations have been elucidated.[46,47,50,52] The disease is most often diagnosed late and there is a poor response to treatment possibly due to poor compliance or non-availability of any form of treatment. These factors are further compounded by poor awareness and low knowledge about glaucoma even by patients. Provider factors include poor facilities and equipment for glaucoma diagnosis and management,[53] inadequate number of ophthalmologists[162] and support teams and limited treatment options (e.g., lasers and trabeculectomy with adjunctive antimetabolites).

In order to reduce morbidity from glaucoma, a public health approach is needed for control and particularly targeted to those at risk. Possible solutions have been proposed and some are being implemented.[46,50,61,62,163] Approaches for control include: To increase public health education for awareness about glaucoma; to improve case-detection methods including opportunistic eye examinations; to encourage case-finding in first-degree relatives; to increase treatment options and availability of medications and surgery; to increase education and training for skilled glaucoma surgeons, patients' counselors and other glaucoma care workers; and to strengthen infrastructure of eye care centers and other systems for glaucoma diagnosis, treatment, and counseling of patients. These should be incorporated into existing Vision 2020 programs and blindness control strategies; and glaucoma care needs to be given high priority.

Further research

Despite the many challenges facing SSA, there is a need to streamline glaucoma control activities and provide evidence-based care. The process to undertake such research can be scheduled systematically and tailored according to local needs and available pooled resources. In the longer term, results and output of the research will be beneficial.

Epidemiological research

More population-based research is needed to clarify the nature of glaucoma in many more populations in Africa, to determine reasons for its variation and to better define target risk groups.

Social sciences/qualitative research

This is important in order to identify the factors and barriers to awareness and knowledge of blinding eye diseases; and compliance and adherence to treatment of glaucoma in SSA.

Clinical care and outcomes

Operational and clinical research for patient care is needed to define clinical guidelines (including issues of patient-physician contact frequency) and protocol of management for optimum glaucoma care. Monitoring of outcomes tools including patient reported outcome and experience measures[164] and quality of life and visual function measures need to be developed. Randomized control trials are needed to define appropriate choices of treatment and provide evidence-base for best clinical care.

Health systems research

Studies that also provide evidence for policy makers and management to facilitate systems for the management of the disease are important.

Health economics research

This will define issues such as cost-benefit of the different options of glaucoma treatment, the economic burden of the disease and health insurance coverage for glaucoma patients.

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Chapter 3

Study rationale, research questions, study aim and objectives

Some members of the Nigeria Blindness Survey team at Idanre Hills, SW Nigeria

Linking material summarising rationale of the study, research questions, and study aim and objectives

Glaucoma - the silent thief of sight

In my early days as a resident ophthalmologist, we organised a glaucoma awareness week. As part of the activities we had a TV programme. First thing the following morning, Mr CJ, a Judge of the high court, came to our hospital. He was well educated and high up in his career. Referring to the TV programme, he said to the Chief Medical Director "your doctors made me to come here today". He had watched the TV programme in which a colleague advised to check one's vision by covering one eye at a time. Mr CJ had lost vision in his left eye and had not realised it until that moment he watched on TV and checked his vision by covering one eye at a time. He had advanced glaucoma. Then, it struck me for the first time, that indeed, glaucoma silently steals away eyesight without the person realising it.

Many years later, while on the Nigeria national blindness and visual impairment survey (thereafter referred to as Nigeria Blindness Survey), we saw many people with glaucoma. We had a service to restore vision to the cataract blind that we encountered, but we could not do so much for the glaucoma persons we saw.

3.1 Rationale of the study

This thesis provides the baseline epidemiological data on glaucoma prevalence in Nigeria. It reports the association between potential risk factors for glaucoma and glaucoma blindness. It also studied issues of management and control of glaucoma blindness from the physicians' perspective, and in the context of patients' understanding and community/public awareness of the disease.

The study involved three main components: (1) Assessing the level of need for glaucoma services; (2) Identifying available services and the constraints involved; and (3) Understanding access to glaucoma care by the population.

This thesis includes a secondary analysis of the relevant data from the Nigeria Blindness Survey in order to enable assessment of the level of need for glaucoma services and identify high-risk groups. The analyses of the Nigeria Blindness Survey data would further clarify ethnic, geographical and socio-economic variations in the disease pattern and provide baseline data for planning delivery of care to glaucoma patients in Nigeria and countries with similar ecological characteristics in sub-Saharan Africa. The Nigeria Blindness Survey data were also analysed to identify factors associated with blindness among those affected so that these groups can have specific early case-finding eye examinations and be offered enhanced health education when they attend services. These data were previously not available.

The second section of the thesis outlines the barriers of giving glaucoma care. Identifying how glaucoma is currently being managed in Nigeria identifies how services can be improved and areas for intervention, including training, in order to define clear, safe and feasible care-pathways in practice patterns. The information about cost of treatment has therapeutic and economic implications. Such analysis in Nigeria would be useful in influencing policy on glaucoma care especially in terms of availability and cost of medication and treatment.

The third section sought to understand why people with glaucoma present late for treatment. Additionally, understanding what patients know and do about glaucoma and public awareness for the disease will facilitate health education strategies to be more relevant in improving awareness of glaucoma in the community leading to better access to care and control of visual loss and blindness from glaucoma.

3.2 Research questions

1. How many people have glaucoma in Nigeria and what are the risk factors for glaucoma and glaucoma blindness in Nigeria?

2. How are physicians in Nigeria diagnosing and treating glaucoma and what constraints do they face?

3. Why do people with glaucoma present late for treatment?

4. Why do people with glaucoma present late and what do the public, and patients with glaucoma know, do and think about the disease?

3.3 Aim

The overall aim of the glaucoma in Nigeria study is to determine ways in which to improve service delivery for glaucoma care in Nigeria.

3.4 Objectives

1. To analyse the Nigeria survey data to estimate the prevalence and describe the types of glaucoma in adults aged 40 years and above in Nigeria.
2. To determine potential risk factors for glaucoma as well as risk factors associated with blindness among those affected.
3. To find out how glaucoma is currently being diagnosed and managed by ophthalmologists/ophthalmic surgeons in Nigeria.
4. To determine the cost of care for glaucoma patients in Nigeria.
5. To determine why people with glaucoma present late for treatment.
6. To identify what the community and patients with glaucoma know, do and think about the condition.

Chapter 4

Study protocol, description of data collection methods; the Nigeria national blindness and visual impairment survey and development of glaucoma diagnosis algorithm

A clinical examination room set up in the community for the Nigeria Blindness Survey

Linking material detailing the study design and protocol, and data collection methods

4.1 Research setting

Nigeria is situated along the western coast of Africa with a surface area of 923,800 square kilometres within latitude 4^0N and 14^0N and longitude 3^0E and 15^0E. Along its southern border is an 800km coastline of the Atlantic Ocean. It is divided into 3 main geographical land areas by the rivers Niger and Benue.

Nigeria became amalgamated as a nation-state in 1914 and became independent from British rule in 1960. There are 374 identifiable ethnic groups with the 3 main ethnic groups being Hausa in the north, Igbo in the southeast and Yoruba in the southwest. The country is divided into six administrative geo-political zones (GPZ), 36 States and the Federal Capital Territory (FCT), and 774 local government areas (LGA).

The 2006 population census indicated a population of 140 million with 18.2% aged 40 years and above. With an average annual growth rate of 2% the population is extrapolated to be 149 million in 2010, and 264 million by 2050. The literacy level is 66.9% and the infant mortality rate is 69 per 1000 live births (2013).

Nigeria has a Revised National Health Policy launched in 2004, and currently being reviewed (2016) with an overall objective “to strengthen the national health system such that it will be able to provide effective, efficient, quality, accessible and affordable health services...” Primary health care (PHC) is regarded as the framework to achieve improved healthcare for the population.[1] However, there is no specific eye health policy and primary eye care is not currently embedded in the PHC framework. The national programme for the prevention of blindness (NPPB) coordinates blindness prevention activities and eye health services of the national Vision 2020 strategic plan. It is a sub-unit in the department of Public Health at the Federal Ministry of Health (FMoH).

4.2 Funding, collaborating institutions and ethical clearance

This PhD study was supported by the Fred Hollows Foundation, Australia through a research degree grant administered by the London School of Hygiene and Tropical Medicine (LSHTM).

Ethical approval was obtained from the Ethics Committee of LSHTM and the Nigeria National Health Research and Ethics Committee (NHREC) (*Appendix 1*). Informed written consent was obtained from participants (*Appendix 5*). Confidentiality was maintained and data obtained would be used only for the purpose of this study and possible interventions arising from it. The study did not interfere with any treatment the patients were receiving at the time of data collection. Participants and other attendees at the community sites found to be in need of further management were referred to the appropriate facility.

The Nigeria national blindness and visual impairment survey (thereafter referred to as the 'Nigeria Blindness Survey), in part, forms the first part of this thesis (Epidemiology of glaucoma in Nigeria). The Nigeria Blindness Survey was a countrywide survey undertaken by the International Centre for Eye Health (ICEH), LSHTM as the major technical partner. Other collaborating institutions for the Nigeria Blindness Survey were Institute of Ophthalmology, London, UK; NPPB, FMoH, Abuja, Nigeria; National Eye Centre, Kaduna, Nigeria; SightSavers International, Country office in Kaduna, Nigeria and the head office in the UK. There was additional support by CBM, Velux Stiftung, and the Federal, State and Local Governments of Nigeria.

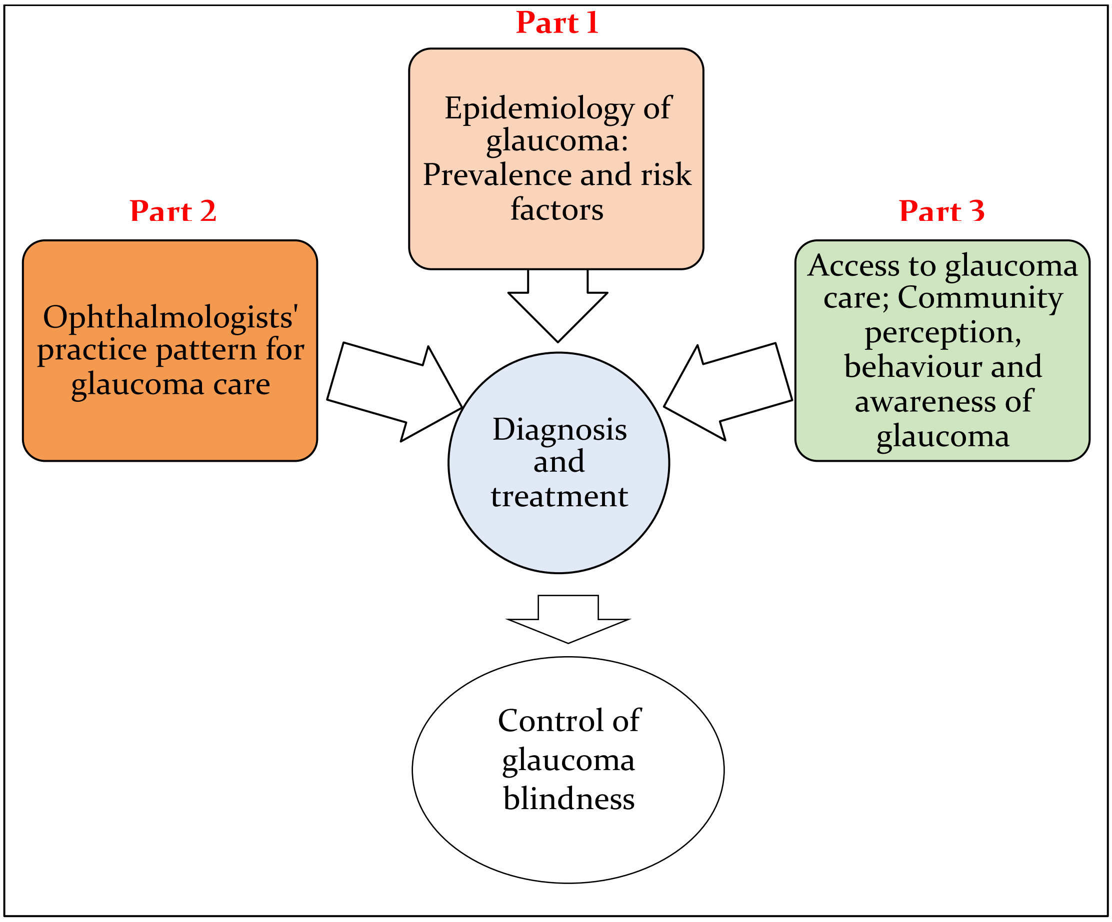
The qualitative study component was undertaken in two selected hospitals and four communities around these hospitals in Abuja, Federal Capital Territory (FCT) and Kaduna State.

4.3 Study design

The overall work has three main parts, which were undertaken separately.

Part 1 describes the epidemiology of glaucoma in Nigeria; part 2 examines glaucoma care provided by ophthalmologists; and part 3 studies access to glaucoma care and the perception, attitude and awareness of glaucoma by patients and in the community. These three components influence the diagnosis and treatment of glaucoma.

Figure 4a: Overview of the study design



4.4 Part 1 – Epidemiology of glaucoma in Nigeria

Purpose: to describe the epidemiology of glaucoma in Nigeria, using data collected during the Nigeria Blindness Survey.

4.4.1 The Nigeria national blindness and visual impairment survey

A Nigeria Blindness Survey was conducted across Nigeria from 2005 to 2007. The survey was prompted by the World Health Organization, as data on blindness from African countries was limited. It was supported by the international non-government organisations that implement prevention of blindness programmes in West Africa so that data could be provided for priority setting and planning eye care services. The methods used in the survey have been described in detail.[2] Ethical approval for the study was obtained from the LSHTM and the Federal Government of Nigeria.

Multistage stratified cluster random sampling with probability proportional to size procedures were used to select a nationally representative sample of 15,027 persons aged $\geq$40 years in 310 clusters across Nigeria (shown in **Figure 4b**). More than 13,500 people were examined. Clinical examination sites were set up in the community. The survey was undertaken by two teams (Team A and Team B) simultaneously in neighbouring States or Local Government Areas (LGAs). Each team comprised one community ophthalmologist as team leader, one clinical ophthalmologist, one optometrist, two ophthalmic nurses, four enumerators, two drivers and a cook. I was the team leader and community ophthalmologist for Team A.

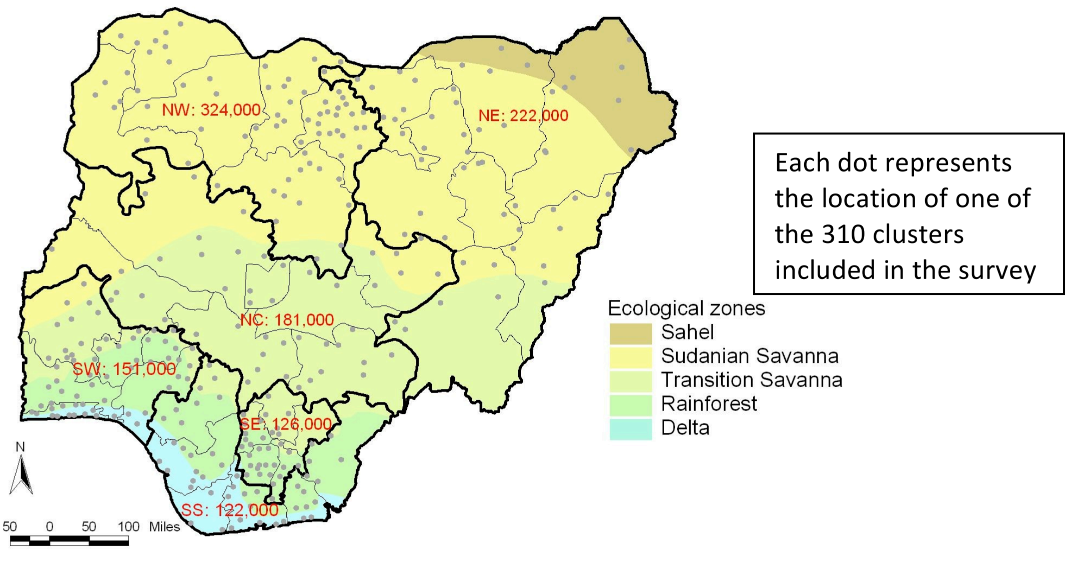
The flow of participants through the survey methods is shown in **Figure 4c**. (See *Appendix 2: Nigeria Blindness Survey data collection form*).

All the participants had their presenting distance visual acuity measured (i.e. with spectacles if usually worn) with the reduced logMAR E-chart and all had FDT visual field testing. This included FDT using the screening test initially which was then run at C20 threshold, when indicated. All those with a presenting visual acuity of <24 letters (Snellen equivalent 6/12) in one or both eyes had a detailed examination which included Goldmann applanation tonometry, Van Herrick's angle grading, gonioscopy if thought to have glaucoma, and dilated fundus examination with digital fundus imaging of the optic disc and posterior pole. All images were graded at the Moorfields Eye Hospital Reading Centre, London (MEHRC).

In addition, 1-in-7 participants also had the full examination and all procedures regardless of their visual acuity, to provide a 'normative' database for Nigerian eyes.

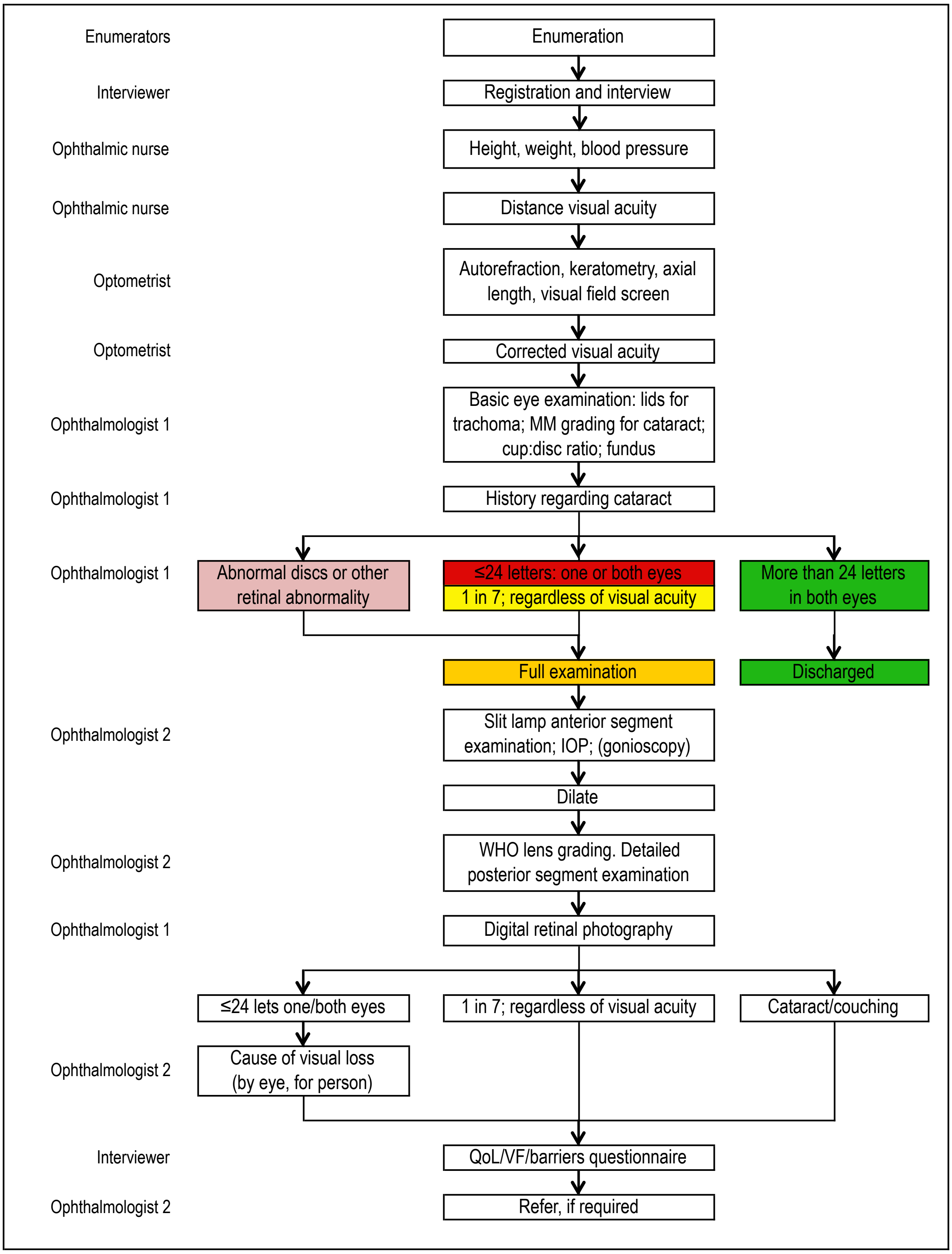
The main findings of the Nigeria Blindness Survey were that the prevalence of blindness was 4.2% (95% CI 3.8 – 4.6%) among those aged 40 years and above,[3] and glaucoma was the second commonest cause of blindness (16.3%).[4] There was marked regional variation in the prevalence of blindness between the dry, less-densely populated north of the country (6.2%) and the rainforest, more urbanised south of the country (2.8%).

Figure 4b: Map of Nigeria showing the states and geo-political zones boundaries, ecological zones and the magnitude of blindness (2008) in the zones



Each dot represents the location of one of the 310 clusters included in the survey

Figure 4c: Flow chart of examination protocol for the Nigeria Blindness Survey



Figures 4d & 4e: The Nigeria Blindness Survey was undertaken in sites/clusters in all terrains

Figures 4f and 4g: A clinical examination room was 'constructed' in this church area in the absence of a suitable building in this community

Figure 4h: The church area (Figure 4f) turned into a clinical examination room for the Nigeria Blindness Survey

The data collected in relation to glaucoma are shown in **Table 4.1**, which also shows a summary of which participants had what examination according to the survey protocol.

Table 4.1: Data collected in relation to glaucoma during the Nigeria Blindness Survey

	Subsets of participants examined			
Parameters	Normal VA "Green cards"	Normal VA "Green cards" with suspect discs (VCDR >0.6, VCDR asymmetry >0.2)	1 in 7 (Normative) "Yellow cards"	VA <24 letters "Red cards"
FDT				
Screening	Yes	Yes	Yes	Yes
Threshold	If failed screening	If failed screening	If failed screening	If failed screening
Disc assessment				
Clinical on-field	Direct funduscopy	Direct funduscopy		
		SLE Biomicroscopy +60D lens	SLE Biomicroscopy +60D lens	SLE Biomicroscopy +60D lens
Digital retinal photos (Dilated pupil)	No	Yes	Yes	Yes
IOP				
GAT	No	Yes	Yes	Yes
RAPD	Yes	Yes	Yes	Yes
AC angle assessment Van Herrick's Angle grading	No	Yes	Yes	Yes
Gonioscopy (Volk's one-mirror non-flanged lens)	No	Yes	Yes If IOP ≥ 20mmHg; VCDR >0.6; VCDR difference >0.2; Van Herrick's grades 0,1,2	Yes If IOP ≥ 20mmHg; VCDR >0.6; VCDR difference >0.2; Van Herrick's grades 0,1,2

VA = visual acuity; VCDR = vertical cup:disc ratio; FDT = frequency doubling technology; SLE = slit-lamp examination; IOP = intraocular pressure; GAT = Goldmann applanation tonometry; RAPD = relative afferent pupillary defect; AC = anterior chamber.

Figure 4i: Registration and interview of enumerated participants

Figure 4j: Visual acuity assessment using the reduced logMAR E-chart

4.4.2 FDT visual field interpretation

Visual field testing was done on all participants except where they were unable to do the test for a variety of psychosocial and pathological reasons. Where FDT readings were not available, the reason was noted. The screening test was initially done and then threshold test done where indicated according to the survey protocol[2] in the presence of clear lens and clear cornea or glaucomatous disc changes (3 criteria: VCDR; VCDR asymmetry; optic disc notch) and/or IOP >20 mm Hg (as agreed by the survey teams).

An algorithm for interpreting the visual field tests results and identifying glaucomatous field defects was formulated. The grading was entered into Microsoft Excel database, which was merged with the existing glaucoma database. The screening mode and the grading options were entered separately for the right eye (RE) and left eye (LE).

Figure 4k: FDT visual field assessment records being sorted for interpretation and grading

The following **codes** were used for visual field data entry:

1. FDT
    1. Done
    2. Not done

2. If not done, indicate why
    1. Uncooperative/ cannot understand/ no coordination/ alertness/ unable to use response button
    2. Visual axis opacity – corneal opacity
    3. Visual axis opacity – cataract
    4. Other ocular pathology
    5. Faulty machine
    6. No electricity
    7. No reason indicated
    8. Other – e.g. home visit
    9. Not applicable (i.e. if FDT done)

3. Screening mode
    1. C20–1
    5. C20–5
    9. Not applicable

4. Screening results (RE/LE)
    1. Normal
    2. Definitely glaucoma
    3. Probably glaucoma
    4. Possibly glaucoma
    5. Not likely glaucoma
    6. Unreliable
    7. Unreadable/illegible records
    8. Missing
    9. Not applicable (also, If threshold test reading available and readable, skip and mark as 9)

5. Threshold mode
    1. Done
    2. Not done (for those that failed screening and should have done a threshold test)
    9. Not applicable (for those with normal screening test or have no FDTs done)

6. Threshold results (RE/LE)

    Interpreted at 3 filter levels of reliability indices: level 0, level 1, level 2 (see details below)

    1. Normal
    2. Definitely glaucoma

    3. Probably glaucoma
    4. Possibly glaucoma
    5. Not likely glaucoma
    6. Unreliable
    7. Unreadable/illegible records
    8. Missing
    9. Not applicable

7. Threshold reliability level

0.	No errors on reliability indices	0% errors
1.	1 error on reliability indices	17% errors
2.	2 errors on reliability indices	33% errors

The following criteria and parameters were used for definitions of normal result and failed screening.

1) Normal screening result

1. No defects
2. 1 or 2 defects at p<1%
3. 1 defect at p<0.5% (only C20-1 has this)
4. 1 or no false positives
5. 1 or no fixation errors

2) Failed screening test – (to have threshold test)

1. 3 or more defects at p<1%
2. 2 or more defects at p<0.5% (only C20-1 has this)

3) Unreliable screening result

All visual field testing equipment depends on the person being tested having the ability to hold steady and on central fixation, as poor fixation can lead to unreliable results. Based on the FDT machine recommendations, the following levels of reliability indices were recorded as unreliable and therefore, the FDT result was not graded:

1. Fixation errors ≥ 2/3
2. False positives ≥ 2/3 * 33% failed reliability indices
3. Brow/Lid positions at lower or upper edges

Three levels of reliability were acceptable and noted in the grading of the FDT threshold results (Nos. 4 to 6 below):

4) Threshold Level 0 reliability * 0% No errors on reliability indices

1. No Fixation errors
2. No False positives
3. Brow/Lid positions at lower or upper edges

5) Threshold Level 1 reliability * 17% errors reliability indices

1. Fixation errors 1 or none
2. False positives 1 or none
3. Brow/Lid positions at lower or upper edges

6) Threshold Level 2 reliability * 33% errors on reliability indices

1. Fixation errors 2 or less
2. False positives 2 or less
3. Brow/Lid positions at lower or upper edges

7) Unreadable/illegible tracings were recorded as such, and were therefore, not graded.

1. Cannot see margins of box
2. Defects seen but cannot assess
3. All tracings faded

8) Missing results were noted where

1. FDT sheet could not be found but FDT marked as done

9) Grading for Abnormal Results

The records of threshold tests were assessed for defects that would increase the certainty of glaucoma diagnosis.

Age-matched normal probability results are same for all threshold tests.

1. Grading was on the defects on the Pattern Deviation Probability (PDP) plot
2. Compared with Total Deviation Probability (TDP) plot

The factors considered in defining defects were

1. Positions of defects: edge or not
2. Depth and size of defects
3. Clustering of defects: adjacent or not
4. Repeatability; if defect is at same location on TDP and PDP plots

4.4.3 Disc parameters (images and clinical assessment)

To determine the VCDR, disc assessment was by direct funduscopy in those with normal VA; stereo-biomicroscope funduscopy with +60D aspheric lens and digital image reading in those with VA <6/12 and every "1-in-7"; and all 3 methods in those with normal VA "green cards" with suspect discs (see **Table 4.1**).

Figure 4l: Slit-lamp biomicroscope funduscopy with +60D aspheric lens

All images were graded at the MEHRC. This was considered the gold standard and was used for analysis. However, in participants whose retinal images were not taken or were ungradable, the clinical records, where available, were used for glaucoma diagnosis. To corroborate the clinical and image VCDR readings, the agreement between the measurement by stereo-biomicroscope funduscopy and digital image analysis was determined (see Chapter 7).

MEHRC grading: For the whole dataset, the discs were classified as glaucomatous or non-glaucomatous based on the 0.7 VCDR rule. Some large cups without glaucomatous changes were classified as not glaucomatous. For the “1-in-7” normative dataset, all images were extracted and re-read to indicate the specific VCDR values. The VCDR readings on this data subset were used to determine the 97.5th and 99.5th percentile values VCDR for the normal population, which were used in the glaucoma diagnosis for Level 1 and Level 2 evidence, respectively.

4.4.4 Intra-ocular pressure (IOP)

The IOP was measured by Goldmann applanation tonometry for participants with VA<6/12 in either eye, the “1-in-7” normative subset and those with normal VA with VCDR >0.6.

The normative subset was used to determine the 99.5th percentile IOP value for glaucoma diagnosis at Level 3 and for where expert opinion would be needed to adjudicate (Level 2b).

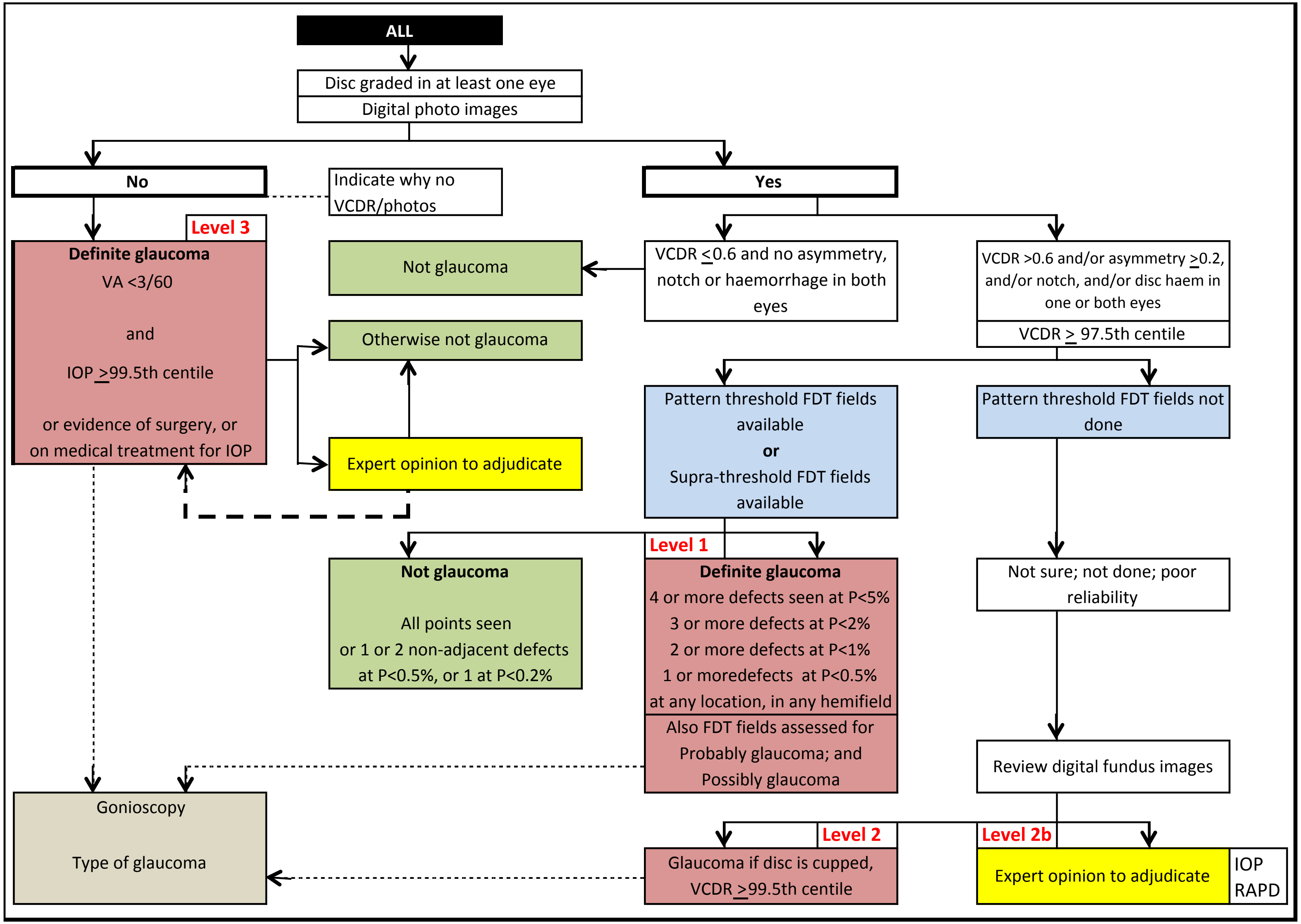
Figure 4m: Goldmann applanation tonometry on a participant at the Nigeria Blindness Survey

4.4.5 Glaucoma diagnostic algorithm

To make the diagnosis of glaucoma, a diagnostic algorithm (**Figure 4n**) was developed based on the ISGEO definition and classification of glaucoma in prevalence surveys.[5] The parameters needed include the appearance and size of the optic discs/cup, IOP, and whether there were characteristic defects in the visual fields. The presence of features suggestive of damage due to the disease, such as disc haemorrhage and notching, and relative afferent pupillary defect were also considered in glaucoma diagnosis.

The "1-in-7" participants who had full ocular examination regardless of their presenting VA formed the normative dataset for analyses to produce the normal percentile values for the parameters required for the diagnosis of glaucoma. Of these, participants who had both VCDR grading on retinal image readings and normal visual fields in both eyes were regarded as the normal population for calculation of the VCDR and VCDR asymmetry percentile values. Participants who had IOP readings and normal visual fields in both eyes generated the percentile values for IOP in the normal population.

Figure 4n: Glaucoma diagnostic algorithm



VCDR = vertical cup:disc ratio; VA = visual acuity; IOP = intraocular pressure; FDT = frequency doubling technology; RAPD = relative afferent pupillary defect.

4.4.6 Data management

Data of the Nigeria Blindness Survey, from all examination sites, relevant to glaucoma were extracted. Grading of the retinal images were entered on Microsoft Excel at MEHRC. Data cleaning of the images was done to resolve conflicts in image labelling. Visual field interpretation and grading results were also entered in Microsoft Excel. These datasets were merged and transferred to STATA/IC 11.0 (Stata Corp, College Station, Texas, USA) using stat transfer to form a single database that was used for the analysis of the Nigeria Blindness Survey data using this software and its subsequent upgrades (STATA 14.0).

The diagnosis of glaucoma in prevalence surveys according to the ISGEO classification[5] was applied. The glaucoma defining centile values for the 3 ocular parameters (VCDR, VCDR asymmetry and IOP) were derived from a normative subset of these data. The data were analysed to estimate the prevalence and magnitude of glaucoma and glaucoma blindness in the study sample and extrapolated to the population. The types of glaucoma were determined by the gonioscopy findings as open angle glaucoma (OAG) or angle-closure glaucoma (ACG); and classified by the absence or presence of an underlying cause into primary or secondary glaucoma, respectively.

Risk factors for OAG and for blindness among adults with glaucoma were determined by socio-demographic characteristics such as age, sex, ethnicity, geographical location, place of residence, socio-economic status, and literacy levels; by ocular/morphological parameters such as ocular axial length, mean ocular perfusion pressure and IOP; by type of glaucoma; and by systemic attributes such as high blood pressure, hyperglycaemia and body mass index.

4.4.7 Data chapters in relation to this aspect of the study

Chapter 5 - Nigeria normative data for defining glaucoma in prevalence surveys

Chapter 6 - A population-based survey of the prevalence and types of glaucoma in Nigeria: The Nigeria National Blindness and Visual Impairment Survey

Chapter 7 - Agreement in measurement of optic cup-to-disc ratio with stereo biomicroscope funduscopy and digital image analysis. Results from the Nigeria National Blindness and Visual Impairment Survey

Chapter 8 - Risk factors for open-angle glaucoma in Nigeria: Results from the Nigeria National Blindness and Visual Impairment Survey

Chapter 9 - Ethnicity and deprivation are associated with blindness among adults with primary glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey

4.5 Part 2 – Glaucoma care by ophthalmologists

Purpose: to describe how ophthalmologists currently manage glaucoma, and the constraints they face

This component of the thesis examined Nigerian ophthalmologists' practice patterns for glaucoma management including their knowledge on cost of therapy. It determined what ophthalmologists do to make a diagnosis and how they treat glaucoma. Quantitative data was obtained from practising ophthalmologists in Nigeria who were given self-administered questionnaires to complete.

4.5.1 Questionnaires completed by practising ophthalmologists

Participants involved and methods of recruitment were in the following order:

1. The databases of the ophthalmological society of Nigeria (OSN), tertiary institutions and the postgraduate ophthalmology training colleges were used to recruit the participants.
2. The participants were all practising ophthalmologists/ophthalmic surgeons qualified by either the fellowship or diploma programmes.
3. Self-administered questionnaires (*Appendix 3*) for collection of quantitative data were distributed and collected at the annual OSN conference held in September 2010 and by personal delivery to those in the same locality as I.
4. Subsequently, questionnaires were distributed and returned by email.
5. Some ophthalmologists completed the questions through telephone interview conducted by the research assistant (MM).

Information about the survey and request for informed consent (*Appendix 4a*) were distributed together with the questionnaire.

Data collected included:

1. Personal/demographic data of respondents
2. Professional/training background
3. Place of practice, type of eye care facility and subspecialty training

4. Care pathway and access to eye care facility by glaucoma patients.
5. Equipment for glaucoma diagnosis and treatment – available/functional.
6. How glaucoma is being diagnosed.
7. How glaucoma is being treated.
8. The types and number of glaucoma surgeries done in a 3-month period and compared to number of cataract surgeries done.
9. The frequency of glaucoma surgical treatment offered as a primary option and compared to medical therapy.
10. Recommended treatment and acceptance rates for treatment recommended.
11. The availability of a recommended standard protocol of glaucoma care in the eye care facility.
12. The availability of patient counselling for glaucoma patients (routine or on request) in the facility.
13. Follow-up arrangement and request for first-degree relatives examination.
14. The cost and availability of glaucoma medications.
15. The cost of glaucoma surgery.
16. Physicians' challenges/fears: training, post-op care, uncertain post-op results, patient acceptance of surgery, etc.

4.5.2 Data management

Data collected for ophthalmologists' practice pattern were entered in Microsoft Excel 2011, transferred to, and analysed with STATA 14.0 (Stata Corp, College Station, Texas, USA). Simple descriptive analysis was undertaken along a systems-oriented approach to determine the pattern of practice of ophthalmologists for glaucoma care.

4.5.3 Data and linking chapters in relation to this aspect of the study

Chapter 10 - Ophthalmologists' practice patterns and challenges in achieving optimal management for glaucoma in Nigeria: Results from a nationwide survey

Chapter 11 - Managing a patient with open-angle glaucoma: a case study

4.6 Part 3 – Access to glaucoma care and community awareness, knowledge and attitude regarding glaucoma

Purpose: To determine why people with glaucoma present late for treatment and what the community and patients with glaucoma know, do and think about glaucoma

Qualitative methods were used to identify the level of public awareness and patients' knowledge, attitudes and beliefs about glaucoma. This component of the study sought to determine:

1. Community/patients' perceptions and awareness of glaucoma.
2. Care-seeking behaviour of participants in terms of what they do when they have symptoms of eye disease/blindness particularly glaucoma.
3. What triggers patients to seek treatment for glaucoma/visual impairment/blindness.
4. The factors that delay presentation at the appropriate health facility.

4.6.1 Participant recruitment and data collection methods

The qualitative study involved various methods:

1. Focus group discussions (FGDs) with participants in four selected communities. This included their positive experiences, as well as the barriers they experienced to accessing eye health care.
2. In-depth interviews (IDIs) with blind persons in the community who had not accessed treatment or had not had successful treatment; preferably glaucoma cases. This took a narrative approach; e.g. "tell me about your blindness…"
3. Direct observations (DOs) of blind persons in the community. This involved observing blind persons to note how their day-to-day lives are affected.
4. Exit interviews (EIs) for glaucoma patients seen by ophthalmologists in the two participating hospitals. They were asked to narrate their experience of their hospital visit and what they felt about the diagnosis and treatment.

Purposive sampling method was employed to select four communities and participants for the FGDs and IDIs. Two communities were selected in the same State as each of two selected hospitals. Selection was based on rural/urban residence, and practical and logistical consideration for the research team in terms of ease of access and language of communication. Language spoken was a key consideration so that the discussions could be conducted/moderated without the need for an interpreter; in order to be as close to the data as possible.

For the FGDs in the community, 13 to 15 participants in a group were invited and informed of the date, time and place of the meeting. Participants invited were: the community leader, community health-worker (if any), and visually impaired and normal sighted residents of the community.

For the IDI, visually impaired and blind participants in the community were selected, some of who had DO.

Patients in the care system were recruited from the two selected participating hospitals for EIs. A designated focal person in the hospitals selected the participants for the EIs. The inclusion criteria were: glaucoma patient aged 25 years and above, undergoing treatment and having just seen a doctor in the clinic.

The data collection instruments used were

- Information sheets
- Consent forms
- Introductory information
- Data collection forms for demographics of participants
- Topic guide
- Note-taking forms: labelling of participants
- Probe for questions
- Voice-recorder
- Camera
- Check-list

Figure 4o: A participant expressing her views in a focus group discussion

Figure 4p: Focus group discussion involving men aged 25 years and above

4.6.2 Topic guide

The development of the topic guide was based on the conceptual framework that knowledge, attitude and understanding would influence early diagnosis and treatment of glaucoma. The topic guide included a series of questions that would bring out the potential factors. The three components of disease perception and awareness (knowledge, attitude and practice) were explored. The probing followed issues that arose in the discussions:

- Explore knowledge and practice
- Explore perception of glaucoma risk: is it serious, treatable, can it resolve on its own
- Determine the concept/understanding of blindness: at what stage of vision to call someone blind; known causes
- Perception of health facility process
- Perception of eye examination and diagnosis
- Perception of treatment of eye diseases, particularly glaucoma, and surgery
- Knowledge of eye health education and awareness carried out
- Triggers that lead to seeking treatment

Themes and guide questions

Knowledge:

- Is the disease recognised? Have you heard about the disease before your diagnosis?
- Do local names exist? For cataract or glaucoma
- Knowledge about the concept of IOP
- Knowledge about the familial tendency. Do you know about risks for family members
- Knowledge about the disease onset and bilaterality
- Is the condition known to be a cause of visual impairment and blindness?

Attitudes:

- Where to find care.
- Is the condition considered serious?

Practice:
- Are there traditional medicines for it?
- Use of eye drops; instillation; its purpose and importance
- Surgery – types, acceptance and purpose
- Do they access available care?
- Timing of presentation to an eye care facility
- What are the triggers for seeking medical care?

Perception of risks:
- Is glaucoma serious?
- Is it treatable?
- Can it resolve on its own?
- Do you consider it as a cause of blindness?

Concept and understanding of blindness:
- At what stage of vision loss do you consider someone to be blind?
- Known causes of blindness
- Diminishing vision part of ageing

Perception of health facility processes:
- How/where to access care
- Who is to give treatment
- Triggers to seeking treatment
- Possible causes of delay in seeking treatment

Perception of eye exam and diagnosis:
- What makes you go for an eye exam

Perception of treatment of eye diseases:
- Especially glaucoma and surgery
- What can be cured – can vision be restored in glaucoma
- Purpose of surgery
- When to have eye surgery

Knowledge of eye health education:
- Know any awareness programme being carried out
- Radio and other media
- At hospital waiting lounge
- In the community
- Key source of information about glaucoma

Cost:
- How much spent

- Direct cost – medicines, surgery
- Indirect costs
- Opportunity cost

For IDIs and EIs, we added the following:

Experience and expectations in hospital

Interventions tried before coming to hospital

What do they do when they have visual symptoms?

Positive experiences

Barriers they experience to accessing healthcare

Narrative: "tell me about your disease/visual impairment/blindness…"

Do you know about risk for family members?

Have you asked any first-degree relative to go for eye examination? If not, why not?

For DOs, our checklist of observations included:

How they interact with their family and members of the community;

How members of the community or anyone that visited approached and related with them;

How independent they are in terms of mobility;

How they use day-to-day gadgets such as mobile phones and telling the time on their watches.

Figure 4q: A participant sobbing as she gives her account of living with glaucoma

Figure 4r: A directly observed participant in his home answering a phone call

4.6.3 Data collection process

For the FGDs, IDIs and DOs in the community, we obtained permission from the community leader. The community-based health workers (fieldwork assistants) identified the communities and participants and a suitable venue for the discussions. Participants were invited on the day of the interviews. Information (*Appendices 4b or 4c; as indicated*) were given, read and explained; and informed consent was obtained (*Appendix 5*). The participants for the IDI and DO were identified at the time of the initial visit to the community, a day before the data were collected. However, they were informed only at the time the interviews took place. The IDI and DO took place in the participant's usual environment, mostly their home in the morning.

For the patients' exit interviews, the permission to conduct interviews was obtained from the hospital authorities. On the day of the interviews, the focal doctor in the hospital selected patients based on the inclusion criteria. They were invited for the discussion and information (see *Appendix 4d*) regarding the study was given and written informed consent obtained from them (*Appendix 5*). The meetings took place in a quiet meeting room in or around the clinic area.
FGDs lasted about 1 hour 30 minutes: introductions/ice-breaking 20 minutes; discussion 50 minutes, rounding up/summary 10 minutes and contact summary 10 minutes. On arrival, participants were welcomed; the group was seated in a circle and demographic information taken. Each was given a label for identification and note-taking purposes. For all interviews, participants were assured that they could stop the discussion at any time if they did not wish to participate and that the tape recorder would be switched off. The recording was then begun and the facilitator followed the topic guide to develop the discussion.

The meetings included introductions, information about FGD/IDI/EI, obtaining informed consent, ice-breaking activities for a few minutes, topic guide discussions, closing remarks and debriefing. All discussions were audio-recorded.

A checklist of some key elements of the interviews were:

Introduction

- General purpose of the study
- Aim of interview/discussion
- Expected duration of interview
- Who is involved
- Cooperation is important
- Information to be collected
- How information will be of benefit
- Any questions can be asked
- Consent obtained

Warm up

- Demographics: Tell us about your name, age, work you do
- Know any persons with difficulty in seeing or with eye disease?
- What is remarkable about them?

Closing remarks

- Is there anything you think is important that we have not talked about?
- Summarise
- Thank participants
- Provide extra information and key contacts to participants

Figure 4s: In-depth interview with a participant in her home

Figure 4t: Conducting an exit interview with a patient in the hospital

4.6.4 Recruitment and training of field assistants

Recruitment and training of field assistants were undertaken before the commencement of data collection. The following field assistants were involved in the qualitative study: a research assistant who also facilitated some interviews, two senior community ophthalmic nurses experienced in community public health awareness and education, a medical social welfare officer involved in counselling for glaucoma patients and two community-based rehabilitation officers.

Training of field assistants addressed overview of the study, aim and objectives, procedures, participant recruitment and interview/discussion techniques and possible challenges and how to overcome them. It also addressed issues on standardisation of data collection, quality control of data collected and skill acquisition for qualitative methodology.

4.6.5 Data management

Identification of study participants, data collection and data entry were done by the study personnel only. Data was accessible only to study personnel. They had access to only the data that they were involved in collecting at the time of the interviews. The data collected were entered into an anonymous database with study numbers as identifiers. The original data collection forms and voice data recordings of the interviews would be archived for 10 years (2012 – 2022).

Audio-recorded data were translated (where applicable), transcribed and entered into NVivo. Data obtained from one FGD was regarded as one set of data even though a number of people gave varying responses. Responses of interest were quantified and patterns of views identified.

The data were analysed using the directed approach to qualitative content analysis to extend the theoretical framework of the glaucoma care pathway. The three main themes were knowing glaucoma, reaching a diagnosis of glaucoma and accessing continued care. Additional codes were applied to identify lived realities and coping mechanisms.

In terms of interpretation, we looked at what would explain these themes and identified structural violence[6, 7] that could be causing people to be in the situation of lack of access to care.

Categories coded at NVivo nodes

There were 3 main themes:

1. Knowing glaucoma
2. Reaching a diagnosis of glaucoma
3. Accessing continued care

Some categories straddle between the three concepts.

'Knowing glaucoma' categories:

1. Misconceptions on causation of eye disease – e.g. in bilateral disease, treatment of 1st eye affects the 2nd eye with the same disease.
2. General lack of knowledge and information about the disease – little knowledge on causes of eye disease
3. Lack of access to information
4. General lack of awareness of the disease
5. Use of alternate nonmedical care

'Reaching a diagnosis' categories:

6. Why aren't people coming for care, for treatment
7. Wait for funding
8. Physical access to healthcare – how the blind and visually impaired get to treatment; distance to appropriate healthcare facility

9. Trust issues for the health system – e.g. frequent tests not understood by patient
10. Cost of finding care – Hopping and hoping
11. Waiting for patients to come to the hospital

'Accessing continued care' categories

12. Cost of purchasing care - Medicines and surgery
13. Debt – contributes to structural violence
14. Hierarchical characteristics of the doctor-patient relationship, one-way communication – e.g. no courage to ask for explanation
15. Unrealistic biomedical instructions – not aware to use medicines for a long time and didn't follow-up so didn't continue with medicines
16. Clinicians and the difficult situation they live in, enormous responsibilities; and expectations from others
17. Doctors still don't know the best way to communicate – (best to have trained personnel do this)
18. How to support the doctors better to practice better – e.g. resource allocation
19. Doctors overworked and too busy to explain to patients
20. Hospital visit experience - language barrier (speak English) at hospitals
21. Constraints in the health system
22. Fear of the effect of vision loss
23. Coping mechanisms – ability to accept consequences based on information provided
24. When people do understand that all we can do is to stop progression. Glaucoma vision loss is irreversible.

Other codes

25. Physical fatigue
26. Financial stress

27. Burden on the family
28. Unwillingness and not being able to talk about their disease - What can be talked about, what cannot – e.g. says she doesn't want to talk about it
29. Relationships – with siblings, neighbours
30. Emotional component – e.g. kept crying
31. Self-blame; have to make own effort; language barrier (speak english) at hospitals; poor follow-up

The 31 categories coded at NVivo nodes were reduced to the following essential points for interpretation and discussion:

Knowing glaucoma

1. Known symptoms
2. Few ocular symptoms – mostly general, not specific
3. Triggers to seeking care
4. Visual symptoms not noticed until late
5. Visual field deficits – linked to disease on hindsight
6. As a cause of blindness – "silent thief" quote
7. General lack of knowledge and information about eye diseases and glaucoma

    a. Poor access to information
        - Where obtained – mostly only radio
        - How information obtained
        - Inadequate information
        - What is needed

Reaching a diagnosis and continued care

8. Cost of care
    b. Finding care - hopping and hoping
    c. Purchasing care – meds, surgery etc., and debts, amount spent

    d. Waiting for patients to come to hospital

9. Hospital visit experience
    a. Physical access to healthcare - how the blind and visually impaired get to treatment
    b. Language barrier - speak English in hospitals
    c. Information on diagnosis and treatment
    d. Accepting treatment options as advised
    e. Unrealistic biomedical instructions; and compliance to treatment - e.g. not aware to use medicines for a long time and didn't follow-up so didn't continue with medicines
    f. Dr/healthcare worker-patient relationship
        - Hierarchical characteristics of doctor-patient relationship – e.g one-way communication, no courage to ask for explanation
        - Clinicians and the difficult situation they live in – enormous social responsibilities, expectations from others
        - Doctors still don't know the best way to communicate or doctors overworked and too busy to explain to patients – best to have trained personnel to do this (quotes of when done)
        - How to support the doctors to practice better – e.g. resource allocation, provision of equipment
    g. Trust issues and constraints in the health system
        - E.g. felt as being held, not being cured and still not being referred to appropriate place of care
10. Treatment of glaucoma
    a. Making choices: Influenced by: severity, age, relatives
    b. Difficulty in appreciating the threat of future sight loss without treatment
    c. Agency – ability to make autonomous decisions
    d. Unable to make informed choice of treatment and continued care, e.g. advice they could not accept
    e. Misconceptions of causation of eye disease – e.g. in bilateral disease, treatment of 1st eye affects the 2nd eye with the same disease.

f. Use of traditional eye medication (TEM)

Lived realities and coping mechanisms

11. Fear of sight loss
    a. Fear of the effect of vision loss
    b. Emotional component – e.g. kept crying
    c. Unwillingness and not being able to talk about their disease - What can be talked about, what cannot – e.g. says she doesn't want to talk about it
12. Loss of economic/social productivity
    a. Employment/retirement and work
    b. Inequality and being left out in socialisation
    c. Self-esteem – feeling of failure, indignity and loss of value to family/community
    d. Relationships with family and neighbours
    e. Physical fatigue
13. Financial stress
    a. Looked after
    b. Wait for funding
14. Coping mechanisms
    a. Faith; Family support
    b. Ability to accept consequences based on information provided
    c. When people understand that all we can do is to stop progression. Glaucoma vision loss is irreversible. Gradual loss of vision – coming to terms with it?
    d. Family – burden on family; family care
    e. For carers: benefits of assisting - Improves bonding, Improves self-esteem, Altruism, Feel good
    f. Relationships
    g. Self-blame; have to make own effort; poor follow-up

15. Other issues
    a. Why aren't people coming for care, for treatment?
    b. They do not feel/know it is their right to access care
    c. No bargaining power
    d. Biological citizenship – e.g. glaucoma patient association

4.6.6 Data chapters in relation to this aspect of the study

Chapter 12 - So let me find my way, whatever it will cost me, rather than leaving myself in darkness: A perception and behaviour study on glaucoma care

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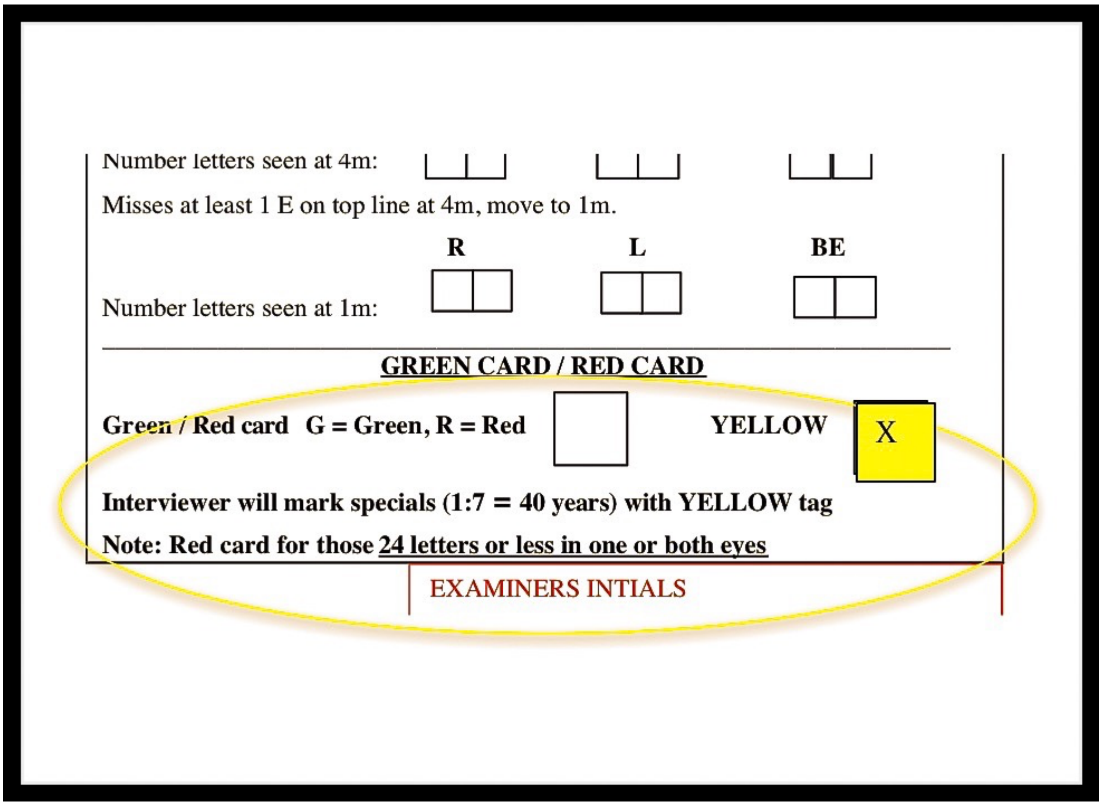
Chapter 5

Nigeria Normative Data for Defining Glaucoma in Prevalence Surveys



Number letters seen at 4m: ☐☐ ☐☐ ☐☐

Misses at least 1 E on top line at 4m, move to 1m.

	R	L	BE
Number letters seen at 1m:	☐☐	☐☐	☐☐

GREEN CARD / RED CARD

Green / Red card G = Green, R = Red ☐ **YELLOW** X

Interviewer will mark specials (1:7 = 40 years) with YELLOW tag

Note: Red card for those 24 letters or less in one or both eyes

EXAMINERS INTIALS

Data systematically derived from 1-in-7 participants provided normative data for comparison

Results paper containing description of the defining parameters for the diagnosis of glaucoma in the Nigeria Blindness Survey data

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SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Ophthalmic Epidemiology		
When was the work published?	March 2015		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	No, *see Appendix 7b*	Was the work subject to academic peer review?	Yes

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Where is the work intended to be published?	
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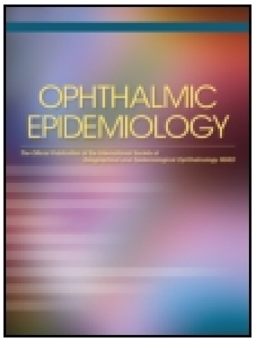
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I collected data as part of the survey team. I interpreted the visual fields data. I performed the statistical analyses. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors.

Student Signature: Kyari **Date:** 28 June 2016

Supervisor Signature: CGilbert **Date:** 30 June 2016



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ORIGINAL ARTICLE

Nigeria Normative Data for Defining Glaucoma in Prevalence Surveys*

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ABSTRACT

Purpose: To determine normative values for defining glaucoma in cross-sectional surveys in Nigerian adults.

Methods: Multistage stratified cluster random sampling with probability-proportional-to-size procedures to select a nationally representative sample of 15,027 persons aged ≥40 years in 305 clusters across Nigeria. Systematic sampling of 1 in 7 participants gave 1759 who were examined in detail to construct a normative database. The normative subset was used to determine values for vertical cup/disc ratio (VCDR) and intraocular pressure (IOP) for glaucoma diagnosis according to the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) criteria. Examinations included visual field testing by frequency doubling technology (FDT), Goldmann applanation tonometry, and optic disc image grading by Moorfields Eye Hospital Reading Centre.

Results: In the normative dataset, 1057/1759 persons (60.1%) had normal FDTs, and constituted the hypernormal. Of these, 851 had VCDR and 973 had IOP measurements taken in both eyes. For category 1 (structural and functional evidence of glaucoma), the 97.5th percentile VCDR was 0.7. For category 2 (advanced structural damage with unproven visual field loss), the 99.5th percentile VCDR was 0.75. In addition, asymmetry in VCDR was 0.1 difference at the 97.5th percentile and 0.2 difference at the 99.5th percentile. Category 3 criteria were used when the optic disc was not visible and field testing not possible; 99.5th percentile IOP is one criterion (28 mmHg).

Conclusion: While these results do not differentiate between open-angle and angle-closure mechanisms, they can be applied to determine the prevalence of glaucoma in Nigeria and sub-Saharan African countries with similar sociodemographic characteristics.

Keywords: Epidemiology, glaucoma, ISGEO, Nigeria, prevalence

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INTRODUCTION

The number of people with glaucoma worldwide was estimated to be 60.5 million in 2010.[1] With an estimated 8.4 million people blind due to glaucoma in 2010 and projected to increase to 11.1 million in 2020, it is the second leading cause of blindness. The Nigerian national blindness and visual impairment survey (thereafter referred to as the Nigeria blindness survey) reported a prevalence of blindness of 4.2% in adults aged 40 years and over,[2] with glaucoma being the second cause, accounting for 16.7% of blindness.[3] Over 180,000 Nigerian adults are estimated to be blind from glaucoma.

Glaucoma is an optic neuropathy associated with characteristic structural damage to the optic nerve and visual dysfunction.[4] These are seen clinically as enlargement of the optic disc cup and loss of visual field, respectively. In order to provide a practical framework for classification of glaucoma in prevalence surveys and also to enable valid comparisons of results between populations, the International Society for Geographical and Epidemiological Ophthalmology (ISGEO) standardized the criteria for classification of glaucoma in prevalence surveys.[4] The defining features in this classification are described according to three levels of evidence, regardless of angle morphology (Table 1). The highest level of evidence is when both structural damage and functional deficits are detected, i.e. a large vertical cup/disc ratio (VCDR) and/or asymmetry between both eyes. An abnormally large VCDR is defined as ≥97.5th percentile of the VCDRs of the normal population in association with characteristic defects in visual fields. Second level evidence is used when visual field testing is not possible, and the diagnosis of glaucoma at this level requires the presence of greater structural damage of the optic disc, i.e. VCDR ≥99.5th percentile of VCDRs in the normal population. The third level is where VCDRs cannot be assessed and visual field testing is not possible, then the diagnosis of glaucoma is based on other clinical parameters in combination; most importantly, intraocular pressure (IOP) ≥99.5th percentile of the IOPs in the normal population, loss of visual acuity attributed to glaucoma, relative afferent papillary defect and medical history (e.g. previous glaucoma surgery). Gonioscopy is included in the ISGEO classification to classify the type of glaucoma according to the mechanism of damage,[4] and is not required for the three levels of evidence for defining glaucoma of all types, as described above.

It is recognized that there is variation in the distribution of optic disc size, VCDR and IOP between populations,[4–37] but there are no data for these values for the normal population in Nigeria. In addition, the Nigeria blindness survey showed that there were considerable differences in the prevalence and causes of blindness between the six geo-political zones as well as between ecological areas.[2,3,38] The prevalence of blindness among those aged 40 years and over ranged from 3.3% (95% confidence interval, CI, 2.4–4.5%) in the southern Delta area to 6.6% (95% CI 4.2–10.4%) in the northern Sahel. The proportion of blindness due to glaucoma varied from 13.2% in the Sudan Savannah to 23.5% in the Sahel.[38] The overall glaucoma-specific blindness prevalence was 0.7% (95% CI 0.55–0.88%)[3] with a 4-fold difference between the ecological areas that have the lowest and highest prevalence, i.e. 0.4% (95% CI 0.2–0.9%) in the Delta and 1.6% (95% CI 0.6–3.8%) in the Sahel.[38] These findings may reflect variation in the incidence or aggressiveness of the disease and/or variation in access to eye care services.

There have only been two, relatively small, population-based surveys designed to estimate the prevalence of glaucoma in Nigeria,[39,40] but neither used standardized criteria to define or classify the condition. The provision of normative data for Nigeria will allow data from subsequent glaucoma prevalence surveys to be compared with other surveys which have used the ISGEO classification, and to elucidate trends over time in response to interventions. The data will also be useful for glaucoma prevalence surveys in other West African countries that have not reported normal values for the defining criteria, and that have similar ecological, sociodemographic and ethnic characteristics.

This paper describes the methods used to derive the normative data for defining glaucoma using population-based data obtained during the Nigeria blindness survey, and reports the distribution of VCDR and IOP for defining glaucoma in prevalence surveys. These values are not intended for use for the

TABLE 1. International Society of Geographical and Epidemiological Ophthalmology (ISGEO) definitions for glaucoma in prevalence surveys (from Foster et al.).[4]

	Parameter				
Level of evidence for the diagnosis of glaucoma	Vertical cup/disc ratio	Visual fields	Intraocular pressure	Visual acuity	Medical history
Category 1	≥97.5th percentile	Typical defect			
Category 2	≥99.5th percentile	Not available			
Category 3	Not available	Not available	≥99.5th percentile	<3/60	e.g. surgery for glaucoma

diagnosis of glaucoma in a clinical setting. The findings have been applied to the whole Nigeria blindness survey dataset to derive glaucoma prevalence estimates and to explore geographical, sociodemographic and ethnic differences, the results of which are the subject of a separate report.

MATERIALS AND METHODS

Study Design

The Nigeria survey was designed to estimate the prevalence and determine the causes of blindness and visual impairment. A nationally representative sample of 15,027 persons aged 40 years and over was selected in 305 clusters across the 36 states and the Federal Capital Territory of Nigeria by multistage stratified cluster random sampling with probability-proportional-to-size procedures. Data were collected over a 30-month period between January 2005 and June 2007 by two clinical teams, each comprising two qualified ophthalmologists, an optometrist, two ophthalmic nurses, interviewers and enumerators. A detailed protocol for all methods was developed and used in training and for reference. Training on clinical assessment was on standardizing method and recording according to the survey protocol and included VA measurement, lens grading, applanation tonometry and optic cup/disc ratio measurement. Quality assurance included on-the-spot supervision by the team leader, daily review of completed questionnaires and data collected, frequent visits to the field by the Project Manager and Project Epidemiologist, inter-observer agreement studies, retraining of all team members before starting the survey in each zone, and double data entry by two trained data entry personnel.

Informed consent was obtained from all participants and community leaders. The study adhered to the tenets of the Declaration of Helsinki and ethics approval was obtained from the Ethics Committee of the London School of Hygiene & Tropical Medicine and the Federal Ministry of Health, Nigeria.

A subsample was used to derive the normative dataset. The subsample was identified by systematically sampling every seventh participant recruited into the study, regardless of ocular findings. These individuals were identified at the registration point by the interviewer and verified by the team leader. They underwent exactly the same rigorous examination procedures as those with visual impairment, as detailed below.

Clinical Assessment

The rationale, objectives and detailed methodology of the Nigeria survey have already been described in detail.[41] A summary of the clinical assessments, with particular reference to data relevant to deriving the distribution and percentile values of VCDR and IOP are described below. Temporary examination sites were set up in the clusters and all enumerated individuals were invited for examination. All participants ($N = 13{,}591$) had their personal and demographic details recorded. Presenting and best corrected visual acuities were measured using a reduced logarithm of the minimum angle of resolution (logMAR) tumbling-E chart[42,43] and categorized using World Health Organization (WHO) definitions of blindness and visual impairment[44] with a further category for near normal/mild visual impairment (<6/12 to 6/18).

Visual field assessment

All participants had visual field testing, after explanation and demonstration, with a Humphrey Frequency Doubling Technology (FDT) visual field analyzer (Carl Zeiss Meditec AG, Jena, Germany). The purpose of the FDT screening test was to identify those without definite or suspected visual field defects (hypernormals). All were screened using the suprathreshold screening mode (C20-1 or C20-5). Prior to conducting the test, images of the test screen and depictions of the flickering of the light seen were used to explain the test. Each eye was tested separately, right then left eye, without correction. The screening test was stopped and restarted or repeated if there were two or three false positives and/or two or more fixation errors. If a participant could not be tested a reason was given, e.g. did not understand the test.

Printouts of all FDT tests were obtained immediately following the test, and data were subsequently extracted and entered into a database. Perimetry results were interpreted using a detailed algorithm (devised and adapted[45–47] by PGS and FK) to define which screened individuals had an abnormal test. The screening test result was considered reliable if there was only one fixation error and/or one false positive (i.e. >33% failed reliability indices).[46] The visual field test was also considered unreliable if there were brow/lid positions at lower or upper edges. A screening test was considered normal if it was reliable (i.e. ≤33% failed reliability indices) and there were no visual field defects; or if there were less than three defects at $p < 1\%$; or less than two defects at $p < 0.5\%$.

Intraocular pressure measurement

Detailed eye examinations included slit-lamp examination (Zeiss SL 115 Classic Slit Lamp, Carl Zeiss Meditec AG, Jena, Germany), assessment for relative afferent pupillary defect and Van Herick's (VH) angle grading. IOP measurement by Goldmann applanation tonometry was performed after instilling topical anesthesia and fluorescein dye (Minims Lidocaine Hydrochloride 4% and Fluorescein Sodium 0.25%, Bausch & Lomb Ltd, UK). A single reading of IOP was measured by the ophthalmologist and recorded to the nearest 1 mmHg. Calibration of the tonometer was verified daily using standard procedures as recommended by the manufacturers. Eyes with significant corneal surface pathology, phthisis or participants unable to fixate were excluded. Central corneal thickness was not assessed.

Gonioscopy and Van Herick's anterior chamber angle estimation

All participants who had a slit-lamp examination also underwent VH anterior chamber angle estimation. Gonioscopy (Volk's 1-mirror non-flanged lens) was performed if IOP was $\geq$20 mmHg, or VCDR $\geq$0.6 or VCDR asymmetry $\geq$0.2, or VH grades were 0, 1, or 2. Gonioscopy and VH grades were used to determine the type of glaucoma by mechanism/angle morphology; findings are reported in a separate paper, and are not the focus of this study.

Optic disc size estimation

Detailed posterior segment examination included dilated optic disc and retinal examination with a 60 diopter (D) aspheric condensing lens (Volk Optical, Inc., Mentor, OH, USA) and binocular indirect ophthalmoscopy (All-pupil binocular indirect ophthalmoscope; Keeler Ltd., Windsor, UK) with a 20D lens. Lens opacities were graded using the WHO grading system.[48] Participants also had digital retinal photography (Zeiss Visucam Lite Desk Top Fundus Camera, Carl Zeiss Meditec AG, Jena, Germany) focused on a mid-point showing the optic nerve head and macular region through a dilated pupil which displays the fundus of the eye at a field angle of 45° showing both disc and macula in the observed field. Reasons for not obtaining images were recorded.

Images were graded independently by Moorfields Eye Hospital Reading Centre using their standard protocol. Images were viewed "full screen" on either a 24″ Eizo S2433W monitor calibrated using a Datacolor Spyder2 calibrator or on a 24″ widescreen Dell 2407WFP LCD monitor calibrated using a GretagMacbeth Eye-One Display 2 calibrator. After determining image quality and clarity, the scleral rim was identified and the boundaries of the disc and the cup were identified using monocular clues such as vascular change in direction. These varied with image quality. Disc pallor gave few clues and was not used. One successful measurement was performed per eye, along the vertical meridian, in Adobe Photoshop (version 7) using the measurement tool, resulting in a cup and a disc diameter value in pixels, along the same plane, the division of the two values producing the VCDR which was recorded to the nearest 0.05. Primary grading was performed by the first reader and inconclusive cases were adjudicated by a second reader.

Magnification of the eye-camera system was determined as described by Bengtsson and Krakau.[49] Parameters included in the formula were axial length measured by A-scan biometry, refractive index of the camera lens (1.336) and a derived camera constant (0.0083) for Zeiss camera magnification (0.5).[50] A correction factor for indentation biometry (0.25 mm) was also applied.[51] The equation assumed that variations in the distance from the apex of the cornea to the posterior principal point of the eye were small, and also assumed that the fundus camera and the ultrasound probe were correctly positioned in relation to the participant's eye. The magnification was applied to the observed vertical disc measurement in pixels and adjusted to obtain estimates of the vertical disc diameter (VDD) in millimeters (adapted from Bartling and colleagues).[50]

A few participants eligible for detailed examination were unable to attend the examination site, and so were examined in their home. In these individuals some investigations were not possible.

Data Analysis

All analyses were undertaken using Stata (Stata/IC 13.0; Stata Corp, College Station, TX, USA). A descriptive analysis of the normative dataset ($n = 1759$) was undertaken. Missing values were excluded. Participants who passed the FDT screening test in both eyes and who did not have visual function abnormalities from other pathology were termed the hypernormal subset. In this subset the population distribution for those with bilateral optic disc grading and bilateral IOP measurements was used to derive the percentile values for VCDR, VCDR asymmetry and IOP. VCDR asymmetry was the absolute value difference of VCDR between both eyes (range 0–1.0). The distribution of these parameters in the whole normative dataset was also determined so as to make comparisons with those in the hypernormal subset.

The strength of the relationship between VCDR and VDD and axial length, and between VDD and axial length was quantified by Pearson's correlation coefficient and linear regression analysis.

The 97.5th and/or 99.5th percentile values for VCDR and IOP in hypernormal persons were analyzed by sociodemographic variables (i.e. age, sex, ethnic group) and place of residence (rural/urban, geo-political zone). Ethnic groups represented by $\geq$100 participants were analyzed separately (i.e. Fulani, Hausa, Ibo, Yoruba). Smaller ethnic groups (<100 participants) were grouped together as "others" and analyzed collectively.

RESULTS

In the ISGEO classification, visual field findings are used to separate category 1 from category 2 evidence. The first step in defining normative values was, therefore, an analysis of the FDT data.

The normative dataset consisted of 1759 participants. FDT testing was conducted in 2889 eyes of 1493 participants (84.9%). Of these, 1396 (79.4%) had both eyes tested; 51 participants (2.9%) had right eyes only tested and 46 (2.6%) had left eye data only. FDT testing could not be done in both eyes of 266 participants (15.1%). Thus FDT testing was not undertaken in 629 eyes of 363 participants (Table 2), the main reasons being poor understanding and inability to use the handheld button (198 eyes; 5.6%). About half of the eyes without visual field results had significant ocular pathology and could not be tested (Table 3).

A total of 1366 (77.7%) of the participants had VCDR image grading at Moorfields Eye Hospital Reading Centre in at least one eye, 1244 (70.7%) of whom had grading for both eyes. Of these, 369 participants (21.0% of 1759) had no fundus photos in both eyes, in about half (187) this was because of a faulty camera and/or generator.

TABLE 2. Number of participants who had FDT visual field screening results, Nigeria.

FDT results	Participants, *n*	%	Eyes, *n*
In both eyes	1396	79.4%	2792
In one eye only	97	5.5%	97
Other eye not tested	–	–	97
Neither eye	266	15.1%	532
Total	1759	100%	3518

FDT, frequency doubling technology.

The Hypernormal Subset

In the 1396 participants with FDT results in both eyes, 1057 individuals (60.1% of 1759) had normal visual fields in both eyes and formed the hypernormal subset (Figure 1).

Percentile distributions for vertical cup/disc ratios

A total of 1101 participants (62.6%) had both VCDR grading and FDT testing in both eyes, 851 of whom (48.4% of 1759) had normal visual fields in both eyes. This subset was used to derive the percentile values for VCDR and VCDR asymmetry (Figure 1).

Overall, there was 99.7% inter-observer agreement for VCDR grading on photos. Regarding quality of the photographs, 72% of images were graded good/adequate for disc field definition for disc assessment. The 97.5th and 99.5th percentile values for VCDR in the hypernormal subset were 0.7 and 0.75 respectively (Table 4). The 97.5th percentile value (0.7) was consistent across all age groups, sexes, places of residence and ethnic groups except in the Fulani and those living in the north-east geo-political zone where the value was 0.6. The 99.5th percentile value (0.75) was more variable, ranging from 0.7–0.85 (Table 5).

In comparison, if all eyes regardless of visual field findings were included, the 97.5th and 99.5th percentile values for VCDR in the normative dataset would be 0.75 and 0.95, respectively (Table 4).

Vertical disc diameter was normally distributed and the estimated mean VDD was 1.29 mm (standard deviation 0.14 mm) with a minimum of 0.85 mm and maximum 1.86 mm. The Pearson's correlation coefficient was 0.36, thus there was a moderate positive linear relationship between VCDR and VDD. The gradient of the linear regression line was 0.40 (95% CI 0.34–0.46). There was also a moderate positive linear relationship between VDD and axial length. Thus, longer eyes had larger disc diameters. However, VCDR was not related to axial length.

TABLE 3. Distribution of participants (and eyes) on the basis of FDT testing, Nigeria.

Reason	Persons, *n*	Eyes, *n*	% of eyes
Had FDT testing in both eyes with normal results	1057	2114	60.1
Could be tested in both eyes but failed FDT screening test	339	678	19.3
Could not be tested in other eye	97	97	2.8
Could not be tested in either eye	266		
Poor coordination of handheld button		198	5.6
Corneal opacity		59	1.7
Cataract		153	4.3
Other ocular pathology		146	4.1
Faulty machine		7	0.2
No electricity/generator		2	0.1
No reason stated		32	0.9
Other, e.g. home visit examination		32	0.9
Total	1759	3518	100

FDT, frequency doubling technology.

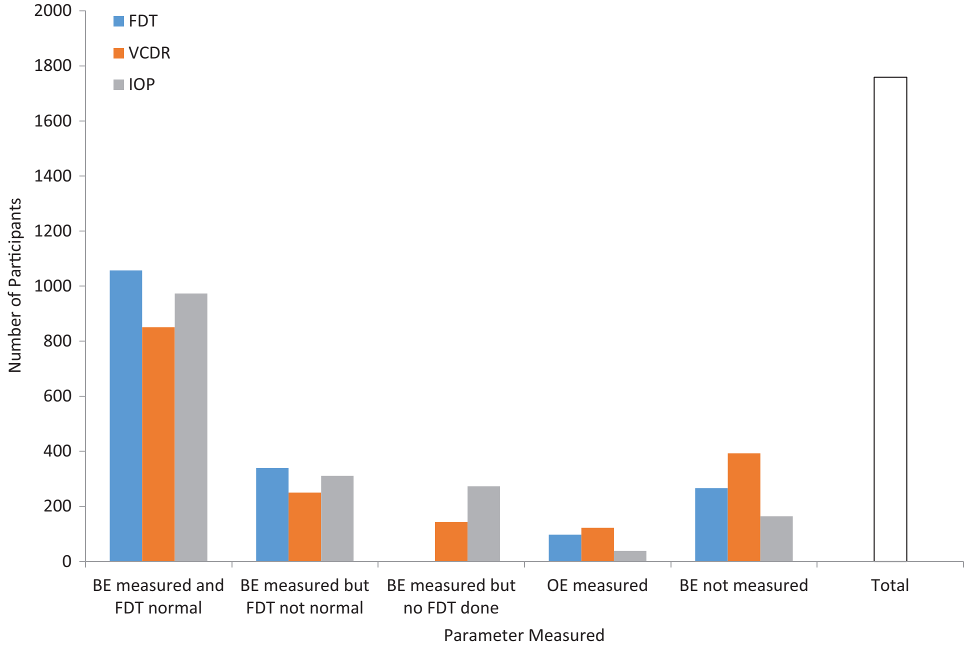

FIGURE 1. Parameters measured in participants recruited to the normative dataset for glaucoma in Nigeria (FDT, frequency doubling technology; VCDR, vertical cup/disc ratio; IOP, intraocular pressure; BE, both eyes; OE, one eye).

TABLE 4. Percentile distributions for VCDR, VCDR asymmetry and IOP in the normative dataset and in the hypernormal subset (normal FDT in both eyes), Nigeria.

Parameter	All eyes of participants with parameter measured (*N* = 1759)			By left and right eyes with normal FDT in both eyes (*N* = 1057)		
VCDR	RE	LE	All eyes	RE	LE	All eyes
N	1308	1302	2610	851	851	1702
0.5th	0.1	0.1	0.1	0.1	0.1	0.1
2.5th	0.1	0.1	0.1	0.1	0.1	0.1
Median	0.4	0.4	0.4	0.4	0.4	0.4
97.5th	0.75	0.75	0.75	0.7	0.7	0.7
99.5th	0.95	0.9	0.95	0.75	0.75	0.75
VCDR asymmetry			Persons			Persons
n			1244			851
0.5th			0.0			0.0
2.5th			0.0			0.0
Median			0.0			0.0
97.5th			0.1			0.1
99.5th			0.3			0.2
IOP, mmHg	RE	LE	All eyes	RE	LE	All eyes
n	1577	1575	3152	973	973	1946
0.5th	7	7	7	8	8	8
2.5th	9	9	9	9	9	9
Median	14	14	14	14	14	14
97.5th	24	24	24	20	20	20
99.5th	36	34	34	28	28	28

VCDR, vertical cup/disc ratio; IOP, intraocular pressure; FDT, frequency doubling technology; RE, right eye; LE, left eye.

The shaded numbers denote the 97.5th and 99.5th percentile values which are relevant for the classification of glaucoma in prevalence surveys.

TABLE 5. Percentile values for vertical cup/disc ratio and intraocular pressure by sociodemographic variables and location of residence, Nigeria.

	Whole study data[a]	Normative dataset	Hypernormal subset	Vertical cup/disc ratio			Intraocular pressure, mmHg	
	n (%)	*n* (%)	*n* (%)	Both eyes *n* (%)	97.5th percentile	99.5th percentile	Both eyes *n* (%)	99.5th percentile
Sociodemographic factor								
Age group, years								
40–49	4889 (36.0)	613 (34.9)	446 (42.2)	373 (43.8)	0.7	0.75	416 (42.8)	22
50–59	3577 (26.3)	464 (26.4)	324 (30.7)	248 (29.1)	0.7	0.75	296 (30.4)	28
60–69	2773 (20.4)	368 (20.9)	198 (18.7)	170 (20.0)	0.7	0.85	185 (19.0)	34
70–79	1653 (12.2)	229 (13.0)	73 (6.9)	50 (5.9)	0.7	0.7	64 (6.6)	26
80+	699 (5.1)	85 (4.8)	16 (1.5)	10 (1.2)	0.7	0.7	12 (1.2)	17
Sex								
Female	7345 (54.0)	939 (53.4)	533 (50.4)	435 (51.2)	0.7	0.75	489 (50.3)	28
Male	6246 (46.0)	820 (46.6)	524 (49.6)	416 (48.9)	0.7	0.75	484 (49.7)	23
Ethnic group								
Fulani	840 (6.2)	108 (6.1)	49 (4.6)	48 (5.6)	0.6	0.75	46 (4.7)	20
Hausa	3375 (24.9)	429 (24.4)	258 (24.4)	218 (25.6)	0.7	0.7	244 (25.1)	28
Ibo	1918 (14.1)	248 (14.1)	128 (12.1)	102 (12.0)	0.7	0.7	120 (12.3)	22
Yoruba	2669 (19.6)	351 (20.0)	226 (21.4)	175 (20.6)	0.7	0.85	193 (19.9)	35
Others	4731 (34.8)	614 (34.9)	391 (37.0)	304 (35.7)	0.7	0.75	370 (38.0)	23
Not indicated	58 (0.4)	9 (0.5)	5 (0.5)	4 (0.5)	–	–	0	–
Location								
Place of residence								
Rural	10,540 (77.6)	1371 (77.9)	809 (76.5)	654 (76.9)	0.7	0.75	737 (75.8)	28
Urban	3051 (22.4)	388 (22.1)	248 (23.5)	197 (23.1)	0.7	0.75	236 (24.2)	34
Geopolitical zone								
North east	1727 (12.7)	270 (15.4)	110 (10.4)	100 (11.7)	0.6	0.75	102 (10.5)	21
South east	1662 (12.3)	211 (12.0)	96 (9.1)	79 (9.3)	0.7	0.7	92 (9.5)	22
South south	1852 (13.6)	241 (13.7)	160 (15.1)	140 (16.5)	0.7	0.7	156 (16.0)	20
North west	3593 (26.4)	402 (22.8)	260 (24.6)	236 (27.7)	0.7	0.75	245 (25.2)	28
South west	2728 (20.1)	362 (20.6)	242 (22.9)	184 (21.6)	0.7	0.85	196 (20.1)	35
North central	2029 (14.9)	273 (15.5)	189 (17.9)	112 (13.2)	0.7	0.75	182 (18.7)	24
Total	13,591 (100)	1759 (100)	1057 (100)	851 (100)			973 (100)	

[a] Eight excluded due to missing data.

Percentile distributions for vertical cup/disc ratio asymmetry

The 97.5th and 99.5th percentile values for VCDR asymmetry in the hypernormal subset were 0.1 and 0.2, respectively. In comparison, if all persons regardless of visual field results were considered, the 97.5th and 99.5th percentile values for VCDR asymmetry in the total study population would be 0.1 and 0.3, respectively (Table 4).

Percentile distributions for intraocular pressure

Data were available on IOP for 3152 eyes of 1595 participants (90.7%) in at least one eye, of whom 1557 (88.5%) had IOP measurement in both eyes. A total of 1284 participants (73.0%) had both IOP measured and FDT testing in both eyes, of whom 973 (55.3% of 1759) had normal visual fields in both eyes. This subset was used to derive the percentile values in the population distribution of IOP (see Figure 1).

The 99.5th percentile value for IOP was 28 mmHg. This is the cut-off value for category 3 diagnosis of glaucoma according to the ISGEO criteria. In comparison, if all eyes were included regardless of visual field results, the 99.5th percentile value for IOP in the total study population would be 34 mmHg (Table 4). The 99.5th percentile value for IOP in the hypernormal population varied considerably by age and ethnic group (range for both 0.7–0.85).

DISCUSSION

We have described the methods used in the first nation-wide study in Sub-Saharan Africa to derive percentile values for defining glaucoma in population-based surveys. These values are for population-based studies only and not values for diagnosing glaucoma in clinical settings. Additionally, as the results of gonioscopy to determine anterior chamber angle morphology have not been included, this paper cannot differentiate open-angle glaucoma and angle-closure glaucoma. Other morphological features of the optic disc area such as disc hemorrhage, retinal nerve fiber layer defects and peripapillary atrophy considered in the clinical diagnosis of glaucoma have not been included in the ISGEO criteria. The hypernormal population was defined by persons with normal suprathreshold visual fields in both eyes. In this

TABLE 6. Distribution of cup/disc ratio and intraocular pressure derived from the ISGEO categorization in different populations.

		Cup/disc ratio		Cup/disc ratio asymmetry		Intraocular pressure, mmHg	
Study populations	Year	97.5th percentile	99.5th percentile	97.5th percentile	99.5th percentile	99.5th percentile	Reference
African countries							
Nigeria (current study)	2013	0.7	0.75	0.1	0.2	28	–
Kongwa,Tanzania	2000	0.7	0.7	0.2	0.3	30	4,5
Hlabisa, South Africa	2002	0.7	0.9	0.2	0.3	30	6
Temba, South Africa	2003	0.7	0.9	0.2	0.3	30	7
Tema, Ghana	2013	0.73	0.85	–	–	34	8
Asian countries							
India							
West Bengal	2005	0.6	0.6	0.1	0.2	24	9
Chennai	2008	0.7	0.8	–	0.2	30	10,11
Andra Pradesh	2010	0.7	0.8	–	–	$24^{R}/30^{U}$	12
China							
Guangzhou	2006	0.7	0.8	0.2	0.3	24	13
Beijing	2010	0.7	0.8	0.2	0.3	–	14
Inner Mongolia	2011	0.7	0.8	0.2	0.3	23.1	15
Handan	2011	0.7	0.8	0.2	0.3	23.7	16,17
Harbin	2011	0.5	0.6	0.1	0.3	25	18,19
Yunnan	2012	0.7	0.9	0.1	0.3	21	20
Other Asia							
Hovsgol, Mongolia	1996	0.71	0.82	0.2	0.3	–	4,21
Chinese, Singapore	2000	0.71	0.82	0.21	0.32	21	4,22
Malay, Singapore	2008	–	–	0.2	0.23	26.5	23
Indian, Singapore	2013	0.60	0.62	0.13	0.20	24	24
Bangkok, Thailand	2003	0.72	0.86	0.21	0.29	22	25
Tajimi, Japan	2004	0.7	0.9	0.2	0.3	23	26,27
Dhaka, Bangladesh*	2004	0.7	0.85	0.15	0.3	32	28
Meiktila, Myanmar	2007	0.65	0.8	0.3	–	25	29
Kandy, Sri Lanka	2009	0.6	0.75	–	–	24	30,31
Sangju, Korea	2011	0.6	0.9	–	–	19	32
Bhaktapur, Nepal	2012	0.6	0.8	0.1	0.2	20	33
Yazd, Iran	2013	0.6	0.7	0.2	0.2	22	34
Australia							
Central Australia (indigenous Australians)	2012	0.7	0.8	–	–	24	35
Europe							
Reykjavik, Iceland	2003	0.7	0.8	0.2	0.3	–	36
South America							
Piraquara, Brazil	2007	0.7	0.9	0.2	0.3	30	37

*Percentile values include participants without visual field testing. R, rural; U, urban; ISGEO, International Society of Geographical and Epidemiological Ophthalmology.

group, any visual dysfunction from other ocular pathologies, and not just glaucoma, would be excluded. The values are of relevance to Nigeria as well as other countries in Sub-Saharan Africa that have similar sociodemographic and ecological profiles to Nigeria. Even though there were differences demonstrated in the values by geo-political zone and in the Fulani and Yoruba ethnic groups, it is still pertinent that the national values be used even in localized surveys in defined geographical areas in Nigeria.

Other glaucoma studies of normative values in Africa,[5–7] Asia,[10–17,26–28] Australia,[35] Europe[36] and South America[37] report a VCDR of 0.7 to be the 97.5th VCDR for level 1 evidence but there is wide variation in the values for other parameters (Table 6). Some of these studies[9,12,26,27,29–31] used values derived from previous studies in the region. Interestingly, even in this study, there was some variability in the VCDR between ethnic groups. There is a need for more rigorous population-based data from African countries where glaucoma is often the second most frequent cause of blindness after cataract.[52]

It is noteworthy that longer eyes did not necessarily have larger VCDRs. However, as predicted VCDR increased with increasing VDD, VCDR was moderately disc-size dependent. Thus, assessment of VCDR and a diagnosis of glaucoma must be interpreted taking account of disc size, particularly in the absence of visual field testing which provides a definite glaucoma diagnosis.

One of the limitations of this study is that the ''gold standard'' Humphrey field analyzer was not used as all equipment had to be portable. Nevertheless, FDT perimetry in a population-based glaucoma screening study has been shown to be reliably performed and with high specificity.[53] Additionally, in our study, two screening modes were used (C20-1 or C20-5). This arose from a difference in calibration of the FDT machine for one of the two teams. Nonetheless, we normalized the criteria when defining the normal visual field. It is acknowledged that another limitation of this study is that only a single reading for IOP was taken. However, for multiple readings to be meaningful, there has to be some time interval between readings which was not practicable in the context of this large survey. The role of IOP in the diagnosis of glaucoma has been contentious and this is reflected in the ISGEO classification where IOP data are used when disc and visual field data are not available. In this study 99.5th percentile values varied considerably by sociodemographic variables, with the value 28 mmHg being higher than most of the studies in Asia, but more consistent with other studies from Africa[4–36] (Table 6). Some of the variability may reflect the relatively small sample sizes in some subgroups. Central corneal thickness was not measured but it is not a defining parameter in the ISGEO classification. However, central corneal thickness measurement is important because corneal thickness may mask the accurate measurement of IOP, which may be underestimated in persons with thinner central corneal thicknesses as documented in an African-derived population.[54] The use of monocular disc photographs with a mid-point disc-macular field image is a limitation. As the images were not centered on the disc, this may have impacted on disc markings and the results may not be directly comparable to those in other studies that used a different focus point. However, monocular clues were used to assess the disc rim and cup, measurements were taken objectively and the reading was standardized. Measuring the true size of the optic disc relies on many imaging properties such as camera and eye magnification factors, and the distance and position in relation to the participant's eye. Some of these were very difficult or not possible to determine in our study. Thus, the stated VDD were estimates and cannot be compared to VDD observed in other studies. However, since the measurements in all participants were subject to the same constant in deriving estimates, the values of VDD in relation to VCDR remain valid. More studies to determine actual disc size in this population are required.

There is a statistical limitation inherent in the ISGEO classification by using the convention that <5% of normal VCDR is considered significant deviation. However, as VCDR is not normally distributed, in the definition of glaucoma, 2.5% (97.5th percentile) is regarded as the upper limit of normal. In addition, the use of VCDR asymmetry as a second parameter improves the definition of glaucoma.[4] Furthermore, the use of visual fields as another parameter to ascertain abnormality considers visual function in the definition. This scheme identifies the more severe cases of glaucoma and provides the minimum estimate of glaucoma prevalence. In defining glaucoma in population-based surveys, it is important to include a group that may not meet the three levels of evidence by the ISGEO criteria but have other defining features such as relative afferent pupillary defect indicative of severe functional deficit in the absence of visual field tests and large VCDR ≥99.5th percentile. It is also important to note that other parameters should be considered for category 3 diagnosis, when optic disc and visual field assessment are not possible in subjects who have IOP less than the 99.5th percentile (28 mmHg in this report), otherwise the misdiagnosis of these individuals would underestimate the prevalence of glaucoma in the population.

This study has strengths: It was population-based, nation-wide and had a high response rate (90.5%). It had a robust sampling and methodology, with good quality control measures and all participants were examined by ophthalmologists who had additional training for the survey protocol. The normative database was derived by systematic sampling and so was representative of the study population as well as the whole population.

In conclusion, this study gives Nigeria normal standardized sets of values for diagnosis of glaucoma in prevalence surveys without having to extrapolate from other populations. These have been applied to derive glaucoma prevalence estimates in Nigeria. The values will also be useful for comparison between studies and in monitoring glaucoma prevalence in response to interventions, with implications on population cohort studies and glaucoma studies of people of African descent.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Chapter 6

A population-based survey of the prevalence and types of glaucoma in Nigeria

Results from the Nigeria National Blindness and Visual Impairment Survey

Discussing the glaucoma diagnosis algorithm and the project plan to generate evidence for improving services for glaucoma in Nigeria; with the Co-Director ICEH (supervisor) and the CEO, Fred Hollows Foundation (sponsor)

Results paper that determined the prevalence of glaucoma using data derived from the Nigeria Blindness Survey

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SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	BMC Ophthalmology		
When was the work published?	December 2015		
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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I collected data as part of the survey team. I interpreted the visual fields data. I developed the glaucoma diagnosis algorithm. I performed the statistical analyses. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors.

Student Signature: Kyari **Date:** 28 June 2016

Supervisor Signature: **Date:** 3 July 2016

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RESEARCH ARTICLE Open Access

A Population-based survey of the prevalence and types of glaucoma in Nigeria: results from the Nigeria National Blindness and Visual Impairment Survey

Fatima Kyari[1,2*], Gabriel Entekume[3], Mansur Rabiu[4], Paul Spry[5], Richard Wormald[1,6], Winifred Nolan[6], Gudlavalleti V. S. Murthy[1,7], Clare E. Gilbert[1] and On behalf of the Nigeria National Blindness and Visual Impairment Study Group

Abstract

Background: Glaucoma is the leading cause of irreversible blindness worldwide. There tends to be a lower reporting of glaucoma in Africa compared to other blinding conditions in global burden data. Research findings of glaucoma in Nigeria will significantly increase our understanding of glaucoma in Nigeria, in people of the West African diaspora and similar population groups. We determined the prevalence and types of glaucoma in Nigeria from the Nigeria National Blindness and Visual Impairment cross-sectional Survey of adults aged ≥40 years.

Methods: Multistage stratified cluster random sampling with probability-proportional-to-size procedures were used to select a nationally representative sample of 15,027 persons aged ≥40 years. Participants had logMAR visual acuity measurement, FDT visual function testing, autorefraction, A-scan biometry and optic disc assessment. Participants with visual acuity of worse than 6/12 or suspicious optic discs had detailed examination including Goldmann applanation tonometry, gonioscopy and fundus photography. Disc images were graded by Moorfields Eye Hospital Reading Centre. Glaucoma was defined using International Society of Geographical and Epidemiological Ophthalmology criteria; and classified into primary open-angle or primary angle-closure or secondary glaucoma. Diagnosis of glaucoma was based on ISGEO classification. The type of glaucoma was determined by gonioscopy.

Results: A total of 13,591 participants in 305 clusters were examined (response rate 90.4 %). Optic disc grading was available for 25,289 (93 %) eyes of 13,081 (96 %) participants. There were 682 participants with glaucoma; a prevalence of 5.02 % (95 % CI 4.60–5.47). Among those with definite primary glaucoma that had gonioscopy (*n* = 243), open-angle glaucoma was more common (86 %) than angle-closure glaucoma (14 %). 8 % of glaucoma was secondary with the commonest causes being couching (38 %), trauma (21 %) and uveitis (19 %). Only 5.6 % (38/682) of participants with glaucoma knew they had the condition. One in every 5 persons with glaucoma (136;20 %) was blind i.e., visual acuity worse than 3/60.

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Conclusion: Nigeria has a high prevalence of glaucoma which is largely open-angle glaucoma. A high proportion of those affected are blind. Secondary glaucoma was mostly as a consequence of procedures for cataract. Public health control strategies and high quality glaucoma care service will be required to reduce morbidity and blindness from glaucoma.

Keywords: Prevalence, Glaucoma, Epidemiology, Nigeria, Open-angle glaucoma, Angle-closure glaucoma

Background

Glaucoma is the second leading cause of blindness worldwide and the leading cause of irreversible blindness, accounting for 8 % of all blindness, affecting an estimated 3.12 million blind people [1]. A review of relevant population-based surveys of glaucoma, and of blindness and visual impairment in sub-Saharan Africa indicate that glaucoma affects about 4 % of adults aged 40 years and above and accounts for 15 % of blindness [2–4]. Africa is the region with the highest incidence and prevalence of glaucoma, most of which is open-angle glaucoma (OAG) [5, 6], and OAG is more prevalent in the black populations of Africa and Africa-derived populations [7]. Reports also suggest that the most difficult problematic OAG that there is in terms of severity of disease, difficulty in treating it and as a cause of blindness comes from West Africa [2, 3, 8]. Additionally, there tends to be a lower reporting of glaucoma in Africa compared to other blinding conditions in global burden data because surveys in Africa may have had limited diagnostic capacity for glaucoma [9]. The Nigeria national blindness and visual impairment survey (hereafter referred to as the Nigeria Blindness Survey), in which over 13,500 people aged 40 years and above were examined, is a population-based survey that substantially addresses glaucoma prevalence and risk factors. The Nigeria Blindness Survey reported the prevalence of blindness to be 4.2 % (95 % confidence interval 3.8–4.6 %) [10], 16.7 % being due to glaucoma [11]. Glaucoma was the leading cause of irreversible blindness [11] and functional low vision [12].

A standard definition and classification system for glaucoma in prevalence surveys proposed by the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) [13] allows comparison of glaucoma prevalence surveys, further highlighting the variation between populations. Whereas angle-closure glaucoma is more frequent among east Asian populations [6, 14], the black populations of USA [15] the Caribbean [16, 17], and Africa [6, 18–22] have the highest prevalence of open-angle glaucoma with up to 90 % of those affected being unaware that they have the condition [18, 21, 22].

In this study, data from the Nigeria Blindness Survey were analyzed using ISGEO criteria to determine the prevalence and types of glaucoma, to provide data for advocacy, policy and to plan services for glaucoma. However, the ISGEO classification system is not for clinical diagnosis or for assessment for treatment of glaucoma. The percentile values for the vertical cup:disc ratio (VCDR), VCDR asymmetry and intraocular pressure (IOP) to define glaucoma were derived from this study population. Possible risk factors for glaucoma in the population are presented in another paper.

Nigeria is the 7th most-populous country in the world and had a total population of 128 million at the time of the national survey (January 2005 to June 2007). Nigeria has 6 main administrative/geo-political zones (GPZ): north-east (NE), south-east (SE), south-south (SS), north-west (NW), south-west (SW) and north-central (NC). Two-thirds (63 %) of the population live in rural areas. Nigeria has more than 250 ethnic groups, who live in different areas in the country each with their own language/dialects, customs and practices. The largest ethnic groups are the Hausa and Fulani in the north, Ibo in the south-east and Yoruba in the south-west. Despite recent economic development, adult literacy levels remain low (51 %), and 54 % of the population live below the poverty line on less than a dollar a day [23].

There are insufficient population-based glaucoma studies in Africa to represent the entire continent in global glaucoma prevalence estimates [6]. From the few high-quality surveys, it is difficult to extrapolate the findings to wider populations as they were conducted in limited and defined geographical areas of large countries [3]. This is the largest truly population-based study of glaucoma in Africa. Estimating the magnitude of glaucoma in Nigeria is important because it sheds light on inter-ethnic and regional variations of OAG prevalence in the black populations of Africa, Caribbean and USA. It will also provide a baseline for planning delivery of care to glaucoma patients in Nigeria and in countries with similar socio-demographic and ecological characteristics in sub-Saharan Africa.

Methods

Details of all the methods used in the Nigeria Blindness Survey have been published [24] as well as data on the prevalence [10] and causes of visual impairment, blindness [11] and low vision [12].

Ethics

Ethical approval was obtained from the Ethics Committee of the London School of Hygiene & Tropical Medicine and the Federal Ministry of Health, Nigeria. Oral informed consent was obtained from community leaders, heads of households and all participants. The study adhered to the tenets of the declaration of Helsinki. Persons with medical or eye conditions needing further assessment and treatment were referred to the nearest healthcare facility. Cataract blind participants were offered surgery after the survey had been completed in each zone.

Sample size calculation and sampling strategy

The sample size calculation was based on the following: target population (22.6 million); expected prevalence of blindness in persons 40 years and older (5 %); desired precision (0.5 %); design effect due to clustered sampling (2); 95 % confidence level; and 85 % response rate. The sample size was 15,375 after allowing for non-response in 310 clusters of 50 participants each. With assumed glaucoma prevalence of 5 % [3], this sample size would also give a precise estimate of the prevalence of glaucoma and allow risk factors for OAG to be analysed.

Multi-stage sampling using probability in proportion to size was used to select a nationally representative sample. In each cluster the center of the village/ward was identified and the direction of enumeration determined by spinning a bottle. Individuals aged 40 years and above who had lived in the household for at least the preceding 3 months were enumerated until 50 individuals had been identified. Examination took place over two days in a temporary clinic set up in the community. Those unable to leave their homes (e.g., due to disability) were examined at home.

Clinical teams and quality control

Data were collected by two clinical teams each comprising of two ophthalmologists, one optometrist, two ophthalmic nurses, four enumerators and one interviewer. Quality assurance included field supervision by the team leader, daily review of data collection forms, frequent visits by the Project Manager (MR) and Project Epidemiologist (GVSM), inter-observer agreement studies, retraining of all team members before visiting each zone, and double data entry by two trained data entry personnel. Three of the four ophthalmologists and both optometrists comprising the clinical teams remained unchanged but different nurses were recruited for each zone in order to address language and cultural variations. A detailed protocol of all the methods was used in training and for reference.

Data collection and clinical assessment

Clinical assessment in relation to glaucoma is described below. The examination flow is shown in Fig. 1.

All participants

All participants had their personal and socio-demographic data recorded including their self-reported ethnic group as well as medical and ocular history, including a history of glaucoma. Height, weight and blood pressure (Omron) were measured. Presenting and best-corrected distant visual acuities (VA) were measured by an ophthalmic nurse with a reduced logMAR E-chart [25]. All participants also had automated refraction, frequency doubling technology (FDT) visual field testing (see below), A-scan biometry by the optometrist and a basic eye examination by the first ophthalmologist.

Detailed examination

The following participants underwent detailed eye examination by the second ophthalmologist [10, 24]: those with a presenting VA <6/12 in one or both eyes; VCDR ≥0.6 in one or both eyes or VCDR asymmetry of ≥0.2, or any retinal abnormality seen on non-dilated direct ophthalmoscopy. In addition, 1-in-7 participants also had the detailed examination regardless of their VA, with random blood glucose testing, to provide a 'normative' database. Detailed eye examination included slit-lamp examination (Zeiss SL 115 Classic Slit Lamp, Carl Zeiss Meditec AG Jena Germany), Van Herick's (VH) anterior chamber (AC) angle depth estimation [26], assessment for relative afferent pupil defect (RAPD), applanation tonometry (Goldmann), lens opacity grading using the World Health Organization (WHO) classification, fundus and optic disc examination with 60D aspheric condensing lens (Volk) and binocular indirect ophthalmoscopy (BIO; Keeler all-pupil) with a 20D lens, and digital fundus imaging with Zeiss Visucam Lite Desk Top Fundus Camera (Carl Zeiss Meditec AG Jena Germany) focused on mid-point between the optic nerve head and the macular region through a dilated pupil. All images were graded independently at the Moorfields Eye Hospital Reading Centre (MEHRC). Gonioscopy (Volk's 1-mirror non-flanged lens) was performed if the IOP was ≥20 mmHg, or VCDR ≥0.6, or VCDR asymmetry ≥0.2, or VH grades 0, 1, 2. Central corneal thickness was not assessed.

Visual field testing

Visual field testing was performed with a Humphrey FDT visual field analyzer (Carl Zeiss Meditec AG Jena Germany). The FDT perimeter is a robust, portable, self-contained unit that weighs less than 10 kg and has a self-calibration procedure. It is generally inexpensive, easy to understand and quick to perform the test [27]: it takes about 45 s to complete a normal screening test and about 45 s for a normal threshold test. These features informed the choice of the FDT perimeter and were advantages considering the logistics of a large population-based survey of this kind where examinations were carried out in

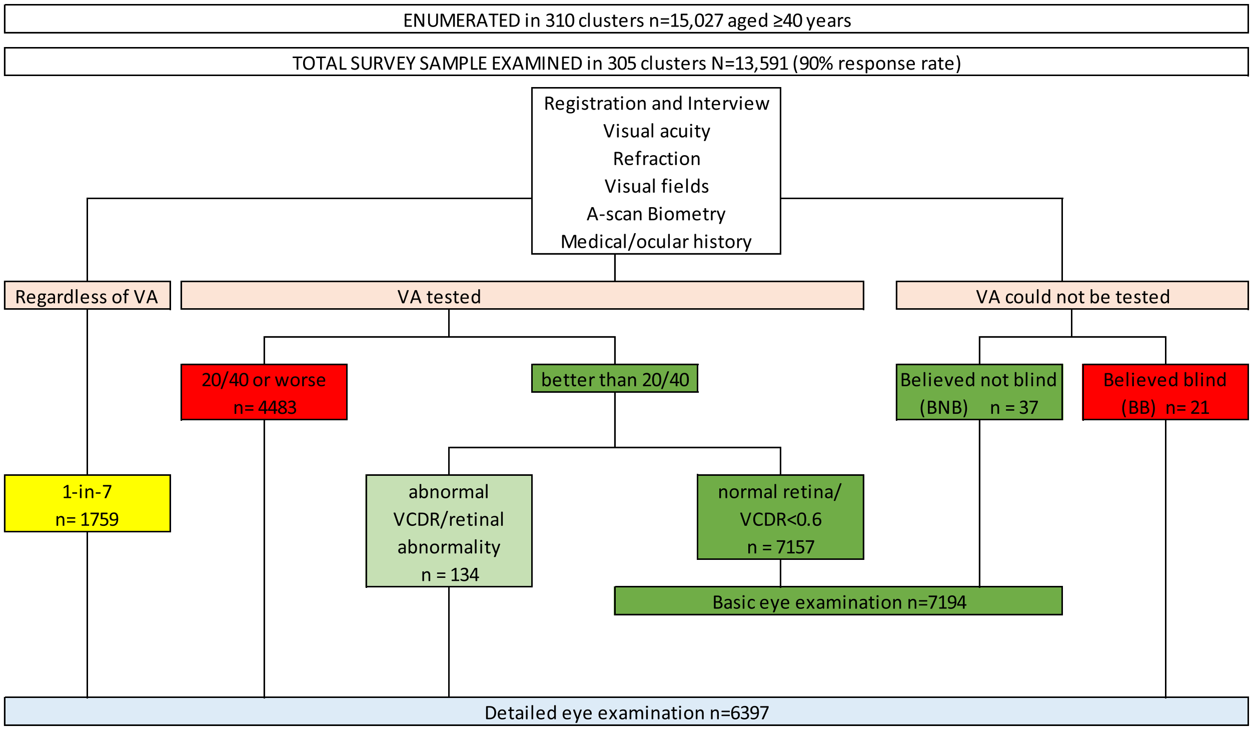


Fig. 1 Examination flow chart for study participants in the Nigeria national survey of blindness and visual impairment. VA = visual acuity; BNB = believed not blind; BB = believed blind, VCDR = vertical cup:disc ratio. Basic eye examination: (n=7194)- Pen-torch anterior segment examination, non-dilated direct ophthalmoscopy. Detailed eye examination: (n=6397) - Slit-lamp examination, WHO lens grading, Van Herick's anterior chamber angle depth estimation, applanation tonometry, gonioscopy if indicated, dilated ophthalmoscopy, digital retinal photography

temporary examination centers set up in the community. FDT utilizes a vertical sine wave grating of low spatial frequency (0.25 c/deg) with counterphase flickering at a high temporal frequency (25 Hz) [28]. All participants were screened using the suprathreshold (C20-5 or C20-1) screening mode after explaining the test and running a demonstration. Each eye was tested separately without correction. The reliability indices considered were fixation error and false positive. The screening test was stopped and restarted or repeated if considered unreliable i.e., there were two or three false positives and/or two or more fixation errors. Clinically abnormal tests were not repeated. A threshold test was done if there were ≥3 field defects at $p < 1$ % or ≥2 field defects at $p < 0.5$ %. If a participant could not be tested or could not see the FDT flickering black and white patterns, s/he was classified as having no FDT test and a reason was given e.g., cataract; or did not understand the test. Print-outs of all FDT tests were obtained immediately and data were extracted and entered into a database. Perimetry results were interpreted using a detailed specific algorithm (devised and adapted [27] by PGS and FK) to identify abnormal visual fields and to classify defects as glaucomatous or non-glaucomatous. The criteria used are outlined in Table 1. The FDT result was interpreted by a 1st reader (PM) and validated by a 2nd (FK); any discrepancy was adjudicated (PGS). Screening reliability was defined as ≤1 fixation error and/or ≤1 false positive (i.e., <33 % failed reliability indices) and threshold reliability was defined as ≤2 fixation errors, ≤2 false positives (i.e., ≤33 % errors on reliability indices). Tests were also considered unreliable if there were brow/lid positions showing as uniformly dense artefact along the upper or lower edges of the FDT result chart. Unreliable results were not included.

Threshold test results were used to diagnose glaucoma if available, otherwise screening results were used. Grading used defects on the Pattern Deviation Probability (PDP) plot compared with the Total Deviation Probability (TDP) plot. Screening tests were considered normal if reliable without defects, or there were ≤2 defects at $p < 1$ %; or ≤1 defect at $p < 0.5$ %. Threshold tests were normal if there were no defects at $p < 0.5$ % and $p < 1$ %, or ≤1 defect at $p < 2$ %, or ≤2 non-adjacent defects at $p < 0.5$ %. Factors considered in categorizing defects as definitely, probably or possibly glaucomatous were position, depth and size, clustering (i.e., adjacent or not) and position; and repeatability (i.e., defect in same location on PDP and TDP plots). We could determine repeatability in participants that had both screening and threshold tests. Defects were not likely glaucomatous if 1) there was a highly shaded

Table 1 Definition of glaucomatous visual field defects for level 1 evidence of glaucoma

FDT test defects	Visual fields				
	Normal	Definitely glaucoma	Probably glaucoma	Possibly glaucoma	Unlikely glaucoma[a]
P <5 %	2 or less non-adjacent	4	3	2 adjacent	
P <2 %	1	3	2	1	
P <1 %	0	2	1 non-edge		
P <0.5 %	0	1	1 non-edge		
Comments		At any location in any hemi-field	At one hemi-field	At one hemi-field	If TDP plot is better than PDP plot
Participants with glaucoma	Total				
Number of participants[b]	268 (100 %)	252 (94 %)	6 (2.2 %)	9 (3.4 %)	1 (0.4 %)
Number of eyes	310 (100 %)	283 (91.3 %)	9 (2.9 %)	13 (4.2 %)	5 (1.6 %)

TDP total deviation probability, *PDP* pattern deviation probability

[a] Other evidence of glaucoma noted in those classified as glaucoma

[b] In participants with bilateral glaucoma, the eye with the highest level of evidence is used to classify that person

TDP with normal PDP plot – this diffuse loss could be due to cataract, for example; 2) TDP was normal or better than the PDP plot or 3) there were vertical meridian defects. However, for diffuse defects, other compelling evidence for glaucoma classification were used (see later).

Van Herick's anterior chamber angle estimation and gonioscopy

The VH AC angle estimation was performed at the slit-lamp. The relationship between the corneal slit image and AC depth was graded 0 to 4 [26]. Grades 0, 1 and 2 were grouped as angle closure or likely to close angles; and grades 3 and 4 as open angles. The iridocorneal angle was assessed by gonioscopy without corneal compression and graded as either open angle or closed angle. The anterior chamber angle was classified as open when Schwalbe's line could be seen; and as closed when it could not be seen. In eyes with glaucoma, the correlation between VH grades and gonioscopy was assessed with the kappa statistic.

IOP measurement

Intraocular pressures were measured by Goldmann applanation tonometry using standard methods and recorded to the nearest 1 mmHg. Tonometers were checked for calibration daily according to the manufacturer's recommendation. Eyes with significant corneal surface pathology, phthisis or participants unable to fixate were excluded.

Optic disc assessment

Cup-disc ratios were assessed clinically by direct ophthalmoscopy for all participants during the basic examination, and after pupil dilation in those having the detailed examination using slit lamp biomicroscopy with a 60D lens. Clinical grading was used in analysis for participants that did not have photo VCDR grading. Methods for clinical VCDR grading by the ophthalmologists were standardized during training using standard sets of optic disc photographs and comparing the clinical grading with the VCDR measured on the retinal photo of the participant being observed.

Digital fundus images were graded independently by MEHRC using their standard protocol. Images were viewed "full screen" on either a 24-in. Eizo S2433W monitor or on a 24-in. widescreen Dell 2407WFP LCD monitor. The former was calibrated using a Datacolor Spyder2 calibrator and the latter was calibrated using a GretagMacbeth Eye-One Display2 calibrator. After determining image quality and clarity, the scleral rim was identified and the boundaries of the disc and cup identified using monocular clues such as vascular change in direction. Disc pallor gave few clues and was not used. The VCDR was then quantified. One successful measurement was performed per eye, along the vertical meridian, in Adobe Photoshop (version 7) using the measurement tool, resulting in a cup and a disc diameter value in proprietary units, the division of the two values producing the VCDR which was recorded to the nearest 0.05. Primary grading was performed by the 1st reader (FS) and inconclusive cases, e.g., tilted discs, blurred images, generalized disc pallor, were adjudicated by a 2nd reader (TP) immediately. If a VCDR measurement could not be obtained, this was stated.

Inter-observer agreement for clinical VCDR measurement between ophthalmologists was assessed with the kappa statistic; each participant had two observations with the second examiner blinded to the result obtained by the first examiner. Inter-observer agreement for VCDR grading on photos was also assessed. The Bland-Altman method was applied to assess agreement between the two methods of measurement i.e., by biomicroscope funduscopy (clinical VCDR) and digital image analysis (image VCDR).

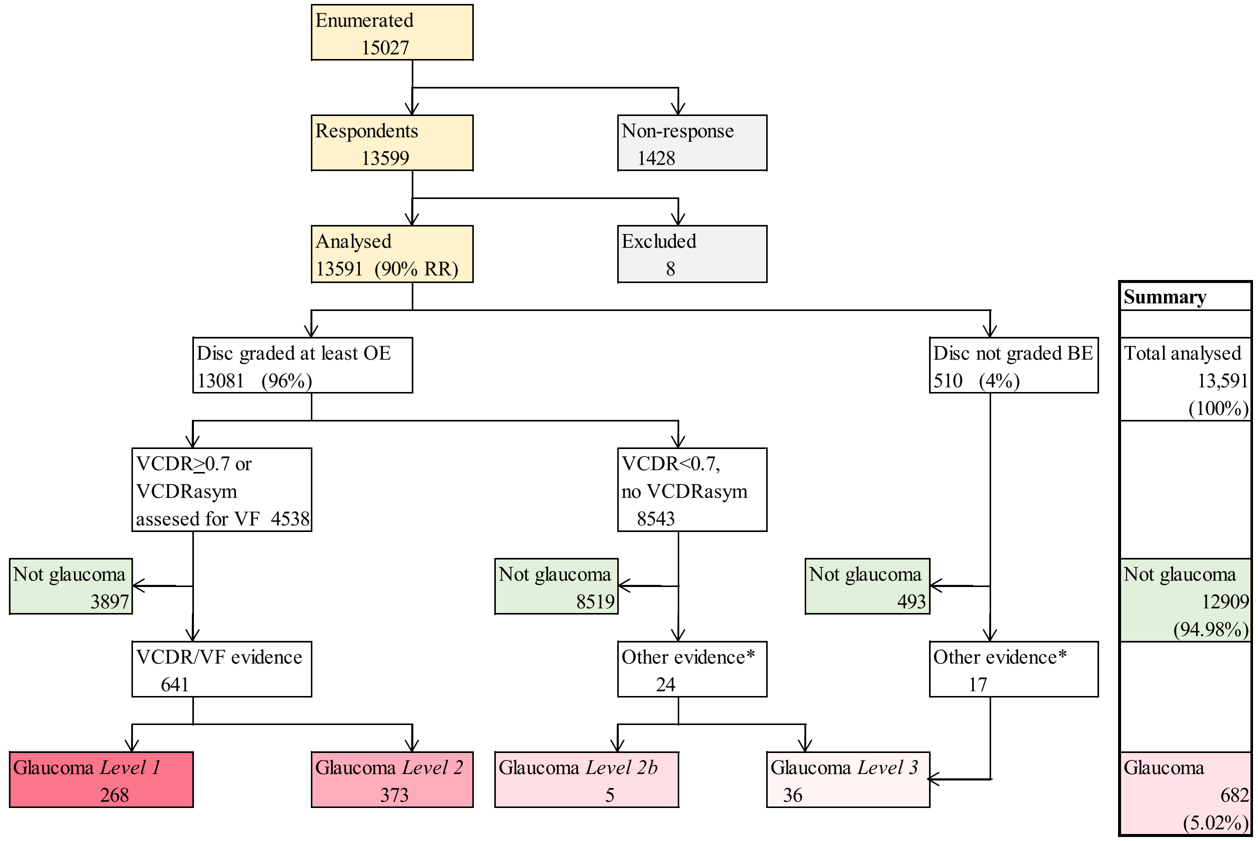
Table 2 International Society of Geographical and Epidemiological Ophthalmology (ISGEO) definitions for glaucoma used in analysis (Adapted From Foster, 2002) [13]

	VCDR or VCDR asymmetry					
Level of evidence	Image reading analysis	Clinical records analysis	Visual fields	Intraocular pressure	Visual acuity	Medical history Other features
Category 1	≥97.5th percentile:	≥97.5th percentile:	Typical defect			
VCDR	0.7	0.6				
VCDR asymmetry	0.1	0.2				
Category 2	≥99.5th percentile:	≥99.5th percentile:	Not available			
VCDR	0.75	0.7				
VCDR asymmetry	0.2	0.3				
Category 2b	≤97.5th percentile: 0.7	≤97.5th percentile: 0.6	±Typical defect	≥99.5th percentile: 28 mmHg		RAPD, Corneal edema
Category 3	Not available		Not available	≥99.5th percentile: 28 mmHg	<20/400	Surgery for glaucoma

VCDR vertical cup:disc ratio, *RAPD* relative afferent pupillary defect

Glaucoma diagnostic algorithm

Glaucoma was classified according to the ISGEO criteria, using percentile distributions of VCDR, VCDR asymmetry and IOP in *normal* Nigerians, derived from the normative dataset ($n = 1759$) of this study population [29] (Table 2). The diagnosis of glaucoma started with VCDR findings (Fig. 2). Category 1 required structural and functional evidence i.e., 97.5th percentile of the VCDR (≥0.7) or VCDR asymmetry (≥0.1) in our normal population and visual field loss typical of glaucoma. Category 2 required advanced structural damage i.e., 99.5th percentile VCDR (≥0.75) or VCDR asymmetry (≥0.2) in the absence of



RR = response rate; OE = one eye; BE = both eyes; VCDR = vertical cup:disc ratio; VCDRasym = VCDR asymmetry; VF = visual fields.
*Other evidence include relative afferent pupillary defect (RAPD), corneal edema, glaucoma surgery, VA<20/400.

Fig. 2 Glaucoma diagnostic algorithm and number of glaucoma participants in each category visual field evidence i.e., when a useful visual field result was not possible or available. Category 3 applied when the optic disc was not seen and visual field testing was not possible, and used: a) blindness (VA <3/60) with the 99.5th percentile IOP (≥28 mmHg), or b) diagnosed with/being treated for glaucoma. An additional level of evidence (level 2b) was added where the optic disc was visualized but the VCDR was <99.5th percentile and visual fields were not available or if visual fields were interpreted as "unlikely glaucoma" but there were other compelling evidence such as RAPD, high IOP and/or corneal edema. Other glaucomatous optic nerve head features such as localized narrowing of the rim, optic disc hemorrhages, and retinal nerve fiber layer defects are not included in the ISGEO classification, and so individuals with these signs only (i.e., no visual field defects; IOP within the normal range for the study population) would not have been classified as having glaucoma. These cases were adjudicated by glaucoma specialists (RW and WN). A person was said to have glaucoma if there was glaucoma in one or both eyes.

Type of glaucoma

Glaucoma was classified as primary and secondary glaucoma. Primary glaucoma was classified as primary open-angle glaucoma (POAG) or primary angle-closure glaucoma (PACG) according to angle morphology viewed by gonioscopy. Glaucoma was classified as secondary where there was an underlying cause such as AC angle neovascularization, exfoliation, pigment dispersion, trauma, surgical procedure, couching or uveitis. The type was unclassified in eyes that did not have gonioscopy.

Data analysis and statistical methods

Visual acuities were categorized using the WHO classification of blindness and visual impairment with addition of a category for mild visual impairment (worse than 6/12 but up to 6/18). The classification uses presenting VA in the better seeing eye. Age was categorized in 10-year groups. Any ability to read and write was classified as literate. Ethnic groups represented by ≥200 participants were analyzed separately (i.e., Hausa, Yoruba, Igbo, Fulani, Kanuri, Nupe, Ijaw, Ibibio, Tiv and Urhobo). Ethnic groups with <200 participants were grouped as "Others" and analyzed collectively. Settlements with a population of ≤20,000 were classified as rural.

The percentile VCDR values used for classification of glaucoma in this study were derived from the photo VCDR grades of the 'normative' data. The percentile values for the distribution of the clinical VCDR records are included in Table 2 for comparison.

Statistical analysis was performed using Stata (Stata/IC 13.0; Stata Corp, College Station, TX). A descriptive analysis of the study population was undertaken. Univariate analysis was performed to describe socio-demographic characteristics (age, gender, ethnic group, literacy and rural/urban place of residence). The age/sex-specific prevalence of glaucoma with 95 % confidence intervals (CI) was calculated taking account of additional variation introduced by the stratified cluster sampling design. Missing values were indicated and excluded in the analysis.

Results

A total of 15,027 adults aged ≥40 years were enumerated in 310 clusters, 13,591 (90 %) of whom were examined in 305 clusters. 6,397 participants had detailed eye examination, 3814 (59.6 %) of whom had images for VCDR assessment in both eyes and 817 (12.8 %) in one eye. Where there was no disc image (2624 eyes of 1329 [20.8 %] participants), clinical VCDR grade was used (Table 3). Reasons why there were no disc images are stated in Table 4. Photos were ungradable if no optic disc features could be assessed due to blur or wrong field definition. Clinical VCDR grades were also used in participants undergoing the basic eye examination only. In the whole study sample, a total of 25,289 (93 %) eyes of 13,081 (96 %) participants had photographic or clinical VCDR grades; 510 (4 %) participants did not have VCDR graded in both eyes (Fig. 2).

Table 3 Summary of completeness of data for participants undergoing full examination (*N* = 6397)

	Eye level data						Person level data			
	Right eye		Left eye		All eyes		One/both eyes		Both eyes	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%
Total	6397		6397		12,794		6397		6397	
Examination										
Van Herick's	5830	91.1	5821	91.0	11,651	91.1	5967	93.3	5684	88.9
Intra-ocular pressure	5496	85.9	5478	85.6	10,974	85.8	5638	88.1	5336	83.4
Disc grading										
Photo	4203	65.7	4242	66.3	8445	66.0	4631	72.4	3814	59.6
Clinical	1320	20.6	1304	20.4	2624	20.5	1329	20.8	993	15.5
None	874	13.7	851	13.3	1725	13.5	–	–	437	6.8

Table 4 Reasons why there was no photo disc grading in 4349 (34 %) eyes among those who had full examination (*n* = 12,794 eyes)

Reason	Right eye	Left eye	All eyes	%
Eye disease				
Cataract	552	469	1021	24 %
Corneal opacity	304	295	599	14 %
Other ocular pathology	166	192	358	8 %
			1978	46 %
Participants factors				
Uncooperative	27	31	58	1 %
Other e.g., home visit	31	27	58	1 %
			116	2 %
Technical reasons				
Faulty camera	471	472	943	22 %
No electricity	144	144	288	7 %
			1231	28 %
Other				
No reason stated	271	312	583	14 %
Ungradable photos[a]	228	213	441	10 %
			1024	24 %
Total	2194	2155	4349	100 %

[a] Photos were taken but VCDR could not be assessed because of blurred image due to media opacity or poor positioning of the participant

The kappa for inter-observer agreement on ophthalmologists' clinical measurement of VCDR within 0.1 was κ = 0.86 (almost perfect agreement) and classifying ≥0.6 or <0.6 was κ = 0.47 (moderate agreement). Overall, the inter-observer agreement between graders for the image VCDR grading at MEHRC was 99.7 %. The Bland-Altman limits of agreement between the clinical and the image VCDR measurements for 95 % of eyes were lower limit of −0.2 to upper limit of 0.3; and 93 % eyes had a difference of ≤0.25 between the two methods of VCDR measurement. In participants undergoing detailed eye examination (*n* = 6397), 93 % and 88 % had VH AC depth estimation and IOP measurement in at least one eye, respectively (Table 3). With 94 % agreement, the kappa for correlation of gonioscopy (closed/open) Vs VH AC (grades 0–2/3–4) in 397 eyes with glaucoma was κ = 0.70 (substantial agreement).

As shown in Fig. 2, 770 participants had VCDR ≥ 0.7 in one or both eyes and a further 3768 had VCDR asymmetry ≥ 0.1, thus a total of 4995 eyes in 4538 participants required visual field analysis (for level 1 evidence) which were available for 3016 (60.4 %) eyes of 2725 (60.1 %) persons. Glaucoma was diagnosed in 63 % (485/770) participants with VCDR ≥0.7/0.75, and in 4.1 % (156/3768) participants with VCDR asymmetry. Other participants were assessed for level 2b and level 3 evidence. The diagnosis of glaucoma was made in a total of 950 eyes of 682 participants - by photo VCDR in 352 (51.6 %), clinical VCDR in 294 (43.1 %) and the disc was not seen in 36 (5.3 %). Thus, glaucoma diagnosis was made by level 1 evidence in 268 (39.3 %), level 2 evidence in 373 (54.7 %), level 2b in 5 (0.7 %) and level 3 in 36 (5.3 %) participants (Table 5).

Table 5 Classification of participants with glaucoma by levels of evidence (as described in Table 2)

	Participants with glaucoma	
Level of evidence	Number of participants	Number of eyes
Category 1		
VCDR	155 (22.7 %)	197 (20.8 %)
VCDR asymmetry	113 (16.6 %)	113 (11.9 %)
Total	268 (39.3 %)	310 (32.7 %)
Category 2		
VCDR	330 (48.4 %)	511 (53.8 %)
VCDR asymmetry	43 (6.3 %)	43 (4.5 %)
Total	373 (54.7 %)	554 (58.3 %)
Category 2b	5 (0.7 %)	10 (1.0 %)
Category 3	36 (5.3 %)	76 (8.0 %)
Total glaucoma	682 (100 %)	950 (100.0 %)

VCDR vertical cup:disc ratio

Prevalence and types of glaucoma

The prevalence of glaucoma of all types was 5.02 % (95 % CI 4.60–5.47 %). The prevalence increased with increasing age and was higher in males, those who were not literate and the Igbo ethnic group (Table 6). These differences were statistically significant. The age-specific prevalence and the magnitude of glaucoma in Nigeria derived by direct standardization with the 2012 Nigeria population are shown in Table 7. There are estimated to be 1.2 million Nigerians aged ≥40 years with glaucoma.

Among the 243 participants with primary glaucoma classified according to pathophysiology based on AC angle morphology by gonioscopy, 208 (86 %) were classified as POAG and 35 (14 %) as PACG (Table 8). PACG was more common in women but the difference was not statistically significant (*p* = 0.08). There were no differences in age, ethnic distribution or rural/urban place of residence between the two groups. Additionally, there was no statistically significant difference in awareness of having glaucoma (*p* = 0.55): 1 in 8 of those with POAG and 1 in 12 of those with PACG knew they had the disease. IOPs were higher in PACG than POAG: the mean IOP was 34 mmHg, standard deviation (SD) 13 in PACG and 27 mmHg, SD 11 in POAG (*p* <0.001).

Table 6 Socio-demographic characteristics of participants with glaucoma in the study population

		Total	Participants with glaucoma		
		N	*N*	%	95 % CI
Total		13,591 (100 %)	682	5.02	4.60–5.47
Socio-demographic factors					
Age group (years)	40–49	4889	93	1.90	1.55–2.33
	50–59	3577	130	3.63	3.03–4.36
	60–69	2773	178	6.42	5.50–7.48
	70–79	1653	178	10.77	9.24–12.52
	80+	699	103	14.74	12.31–17.54
					p <0.001
Gender	Female	7345	328	4.47	3.98–5.00
	Male	6246	354	5.67	5.05–5.47
					p = 0.002
Ethnic group[a]	Hausa	3375	130	3.85	3.00–4.93
	Yoruba	2669	156	5.84	4.94–6.90
	Igbo	1918	149	7.77	6.57–9.16
	Fulani	840	30	3.57	2.53–5.01
	Kanuri	353	18	5.10	3.40–7.58
	Tiv	342	11	3.22	2.29–4.51
	Ijaw	251	15	5.98	4.46–7.96
	Urhobo	245	7	2.86	1.50–5.37
	Ibibio	212	12	5.66	2.35–13.03
	Nupe	211	11	5.21	3.41–7.88
	Others	3117	139	4.46	3.72–5.33
					p <0.001
Literacy	Literate	5925	248	4.19	3.60–4.86
	Illiterate	7666	434	5.66	5.14-6.23
					p = 0.001
Place of residence	Rural	10,540	520	4.93	4.46–5.46
	Urban	3051	162	5.31	4.47–6.30
					p = 0.473
Visual status	Not blind	13,022	546	4.19	3.83–4.59
	Blind	569	136	23.90	20.24–27.99
					p <0.001

CI = confidence interval
[a] 58 missing values excluded

Other findings

Only 5.6 % (38/682) of all participants with glaucoma knew they had the condition. The commonest causes of secondary glaucoma ($n = 53$ participants) were couching (an ancient, traditional non-medical manipulation of the crystalline lens; 38 %), trauma (21 %), uveitis (19 %) and following intracapsular cataract surgery (17 %). Over a third of the eyes with glaucoma (365; 38 %) had a presenting VA worse than 3/60; and 1 in every 5 persons with glaucoma (136; 20 %) was blind (VA worse than 3/60 in the better eye). In 68 % of the 136 blind with glaucoma, the main cause of blindness was attributable to glaucoma. Among the 40–49 year-group with glaucoma, 13 % were blind, and this age-specific proportion of blindness among glaucoma participants increased with age to 30 % in the 80+ years age-group.

Figure 3 shows the distribution of IOP in all eyes: the mean IOP was 14 mmHg, SD 4 in the non-glaucomatous eyes compared to 23 mmHg, SD 12 in the glaucoma eyes. The difference in the mean values was statistically significant ($p < 0.001$). The modal IOP was 12 mmHg in both groups. There were three different peaks at 12, 28 and

Table 7 Age-standardized glaucoma prevalence rates

	Study sample		Prevalence of glaucoma				Magnitude of glaucoma
			Crude rate		Age-adjusted rate[a]		Estimated numbers
	N	%	*N*	%	%	95 % CI	
Age group (years)							
40–49	4889	35.97	93	1.90	1.51	1.96–2.94	166,308
50–59	3577	26.32	130	3.63	3.69	2.98–4.29	232,792
60–69	2773	20.40	178	6.42	8.85	3.99–5.43	318,689
70–79	1653	12.16	178	10.77	16.85	5.91–8.00	321,820
80+	699	5.14	103	14.74	12.32	14.72–20.98	181,807
Total	13,591	100	682	5.02	5.02	4.60–5.47	1,221,416

CI confidence interval

[a] Standardized with the 2012 Nigeria population

50 mmHg in the IOP distribution of the eyes with glaucoma. About half (56 %) of the eyes with glaucoma had IOP ≤22 mmHg. Conversely, 4 % had IOP >21 mmHg but did not have glaucoma.

Discussion

The Nigeria Blindness Survey was the largest, national population-based survey of eye disease in an ethnically diverse, indigenous black African population, giving precise estimates of the prevalence of glaucoma. The sample was nationally representative by age, gender, ethnicity, rural/urban residence and socioeconomic status [24], with a high response rate and the results are generalizable to the whole country and also to people of the West African diaspora around the world whose predecessors were victims of the slave trade e.g., African Caribbean and African American people. Though now genetically mixed to varying extent, our study population is likely to have the same genetic determinants of the glaucoma seen in those populations. Additional strengths are the standardized protocol, the same clinicians and equipment were used throughout the study, and photographic VCDR grading was performed by the MEHRC, an independent, internationally recognized reading center. Furthermore, the centile values for VCDR and IOP distribution in the population used to define glaucoma were derived from the same study population.

Table 8 Proportion of the different types of glaucoma in the Nigeria National Survey of Blindness and Visual Impairment

	Proportion of glaucoma	
Glaucoma type	N	%
All glaucoma[a]	682	100.0
POAG	208	30.5
PACG	35	5.1
Secondary glaucoma	53	7.8
Unclassified[b]	386	56.6

POAG primary open angle glaucoma, *PACG* primary angle-closure glaucoma

[a] All glaucoma prevalence is 5.02 % (95 % CI 4.60–5.47 %)

[b] No data on gonioscopy, thus not classified by anterior chamber angle morphology

The survey indicates that 1.1 to 1.4 million adults in Nigeria have glaucoma, most of whom are not aware that they have the disease. One in every 20 Nigerians aged 40 years and above has glaucoma, and one in five being blind. There are approximately 8500 people aged 40 years and above with glaucoma per million population. The high prevalence and high rate of blindness confirm glaucoma to be of public health importance and should become a priority among healthcare planners and policy makers, emphasizing the need for glaucoma care pathways for early detection and treatment to prevent blindness. In Nigeria, 8 % of glaucoma was secondary, with over half of these following procedures for cataract, particularly couching, which is still widely practiced in Nigeria despite very poor visual outcomes [30]. This underscores the need for high quality, affordable and accessible cataract surgical services. The findings have public health implications for other countries in sub-Saharan Africa which share similar socio-demographic characteristics.

The prevalence of glaucoma in Nigeria is similar to that in Temba, South Africa [20], slightly higher than in South African Zulus [19] and in Kongwa, Tanzania [18] but lower than in Tema, Ghana [21] and Akinyele, SW Nigeria [22]. Although these surveys were undertaken in localized populations, there seems to be an emerging pattern with the prevalence being higher in West Africa than in South Africa which in turn is higher than in East Africa. The Ghana study [21] had a high proportion of Level 1 diagnosis (87.2 %) compared with our study (39.3 %) as in Nigeria there were high rates of cataract and other pathology which precluded visual field assessment. As Level 2 requires evidence of more advanced structural damage our estimates for Nigeria are, therefore, minimum estimates.

The prevalence of glaucoma in Nigeria is lower than that of POAG reported from Barbados (6.7 %, 95 % CI 6.3–7.8) [17], being similar to black populations in the United States of America (USA) [15] but slightly higher than in Asian populations [31–38] and much higher than white populations in the USA [15, 39], Australia [40] and Europe

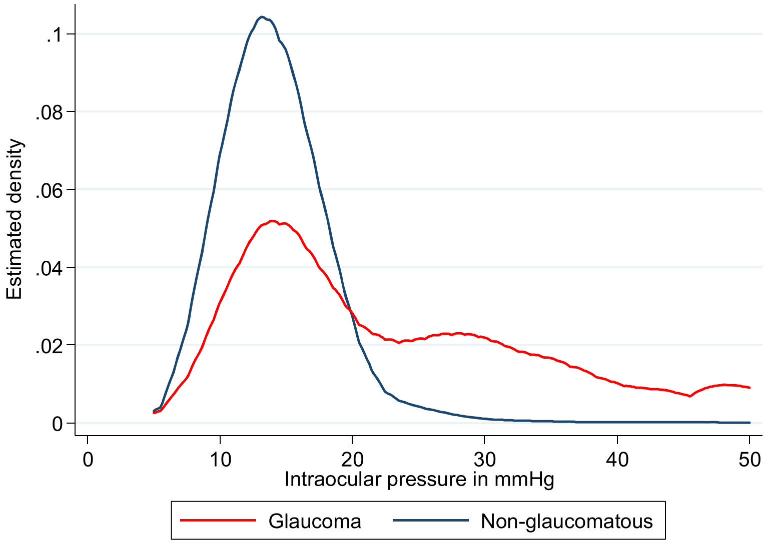


Fig. 3 Distribution of IOP in glaucoma and non-glaucomatous eyes

[41–44]. The prevalence of glaucoma in Nigeria is also higher than in Brazil [45], Iran [46], indigenous populations in Australia [47] and Qatar [48]. Regional/racial variations in prevalence have been attributed to genetic and possible environmental differences [49, 50]. Susceptibility gene loci significantly associated with POAG and genes involved in IOP regulation have been studied in some African populations [51, 52]. In Nigeria, the Igbo, a rather homogenous ethnic group, had the highest prevalence of glaucoma which may also reflect genetic susceptibility.

The relatively high age-specific prevalence of glaucoma in 40–49 year olds in Nigeria and the high proportion of glaucoma blindness suggest severity at an earlier age [15, 17, 21, 22] and more aggressive course [53] in Blacks than in Caucasians [41, 42, 44] and some Asian populations [33, 34] over and above lack of diagnosis and treatment since the high proportions of undiagnosed glaucoma are relatively similar (Table 9). However, this could also be the natural history signifying poor access to treatment. Additionally, because of the earlier age of onset and longer years with untreated glaucoma, the risk of going blind would be much greater. The racial/regional disparity in disease severity may be attributed to additional factors such as inflammation [54, 55] and the different peaks of IOP in eyes with glaucoma may indicate genetic susceptibility at varying levels of IOP. However, these interpretations are speculative and warrant further research.

The classification of glaucoma by pathophysiological mechanism based on angle morphology is important because POAG and PACG have different natural histories and different management strategies. In Nigeria POAG was the commonest type of glaucoma, as reported in other black populations [3, 15–22, 45].

It is acknowledged that communities in Nigeria, where prior diagnosis of glaucoma is low, have extremely little knowledge about glaucoma. Questions were, therefore, not asked on whether first-degree relatives had glaucoma as participants would be highly unlikely to know. In addition, the ISGEO classification does not take first-degree relatives into account.

It is noteworthy that at least half of the glaucoma eyes had an IOP less than the mean +2SD IOP (22 mmHg) of non-glaucoma participants. The important implication is that IOP is unable to differentiate between those with glaucoma and those without glaucoma.

A limitation of this study is that the ‘gold standard’ Humphrey field analyzer was not used as, unlike the portable FDT perimeter, it would not have been feasible to transport it to all examination centers especially in the terrain and environment of the survey. Nevertheless, we had an acceptable and reproducible test of visual function based on the central 20° field of vision. Another limitation was that pachymetry was not done. The data would have added more information on corneal thickness in relation to glaucoma. Interestingly, in the Barbados Eye Studies, corneal thickness tended to be thinner in the black participants than in the white participants but was not correlated to IOP [56]. However, as corneal thickness decreased, there was a higher likelihood of incident OAG [57]. Also, not all participants had dilated disc assessment or photographic disc grading as this was not possible given the large sample size of the study. The fundus camera produced non-stereoscopic images and monocular clues were used to determine optic disc and cup boundaries. Though this may have led to misclassification, most of the cases classified as glaucoma in this survey were “barn-door”. Even though there is a tendency for non-stereoscopic

Table 9 Prevalence of Glaucoma in some population-based studies for age ≥40 years

Study population	Examined (response rate %)	Prevalence of glaucoma			Undiagnosed glaucoma (%)	Proportion blind (%)	Reference
		n	All glaucoma % (95 % CI)	40–49 years age-specific			
Nigeria, National	13,951 (90)	682	5.0 (4.6–5.5)	1.9 (1.6–2.3)	94	20	This study
Africa							
Kongwa, Tanzania	3247 (89)	135	4.2 (3.5–4.9)	1.7 (1.1–2.5)	98	14	[18]
Hlabisa, South Africa	1005 (90)	41	4.5 (3.2–6.1)	1.2 (0.2–3.4)	90		[19]
Temba, South Africa	839 (75)	55	5.3 (3.9–7.1)	1.1[b]	87		[20]
Tema, Ghana	5603 (82)	32	6.5 (5.8–7.1)	3.2 (2.7–4.1)	97	3	[21]
Akinyele, Nigeria	811 (90)	59	7.3 (5.5–9.1)	4.6 (2.1–7.1)	90	6	[22]
Asia							
Qatar	3149 (97)	67	1.7 (1.7–1.8)	1.45 [b]	51	6	[48]
Yazd, Iran	1990 (86)	87	4.4 (3.3–5.4)	1.6 (0.8–2.4)	90		[46]
Chinese, Singapore	1232 (72)	45	3.2 (2.3–4.1)[a]	1.1 (0.2–4.8)	62		[31]
Chinese, Singapore	3353 (73)	134	3.2 (2.7–3.9)[a]	0.7 [b]	85	10	[38]
Malay, Singapore	3280 (79)	150	3.4 (3.3–3.5)[a]	2.2 [b]	92	10	[36]
Indian, Singapore	3400 (76)	78	1.9 (1.5–2.5)[a]	1.3 [b]	72	10	[35]
Beijing, China	4439 (83)	158	3.7 (3.1–4.2)	2.2 (1.5–3.0)	-	2	[37]
Kailu, China	5197 (87)	169	2.9 (2.0–3.8)[a]	2.0 (1.3–2.7)	66	7	[32]
Bhaktapur, Nepal	3991 (83)	75	1.8 (1.7–1.9)[a]	0.3 [b]	96	2	[33]
Central India	4711 (80)	122	3.5 (2.8–4.1)	1.0 (0.5–1.6)	–	1	[34]
Australia							
Indigenous, Australia	1061 (64)	26	2.2 (1.6–3.6)	1.5 (0.4–2.5)	81	12	[47]
Europe							
Ponza, Italy	1034 (84)	39	3.8[b]	0 (0.0–1.7)	–		[42]
Egna-Neumarkt, Italy	4297 (74)	121	2.9[b] approx	0.5 [b]	–		[41]
Wroclaw, Poland	4853 (83)	79	1.6 (1.3–2.0)	0.4 (0.1–1.1)	71		[44]

CI confidence interval
[a] Adjusted rates
[b] 95 % confidence interval not reported
– no data

assessments to yield slightly varied optic disc parameters [58, 59], these differences were inconsistent and the agreement between stereoscopic and non-stereoscopic VCDR assessment were generally extremely good and repeatable [58]. A further limitation was that the fundus camera was not calibrated for disc size so VCDRs could not be adjusted for disc size. Technical difficulties in the field (faulty camera or generator) meant that disc images were not obtained in 616 participants when needed. High humidity damaged the mirror coating of gonioscopy lenses so that some eligible participants did not have gonioscopy performed and VH AC angle estimation was used instead. Hence, the proportions for angle-closure glaucoma and open-angle glaucoma were obtained only from participants that had gonioscopy. Additionally, lack of indentation gonioscopy, use of a one-mirror gonioscopy lens, and defining open-angle glaucoma as a visible Schwalbe's line may have led to some misclassification of the type of glaucoma. The survey protocol indicated detailed eye examination of those with VCDR asymmetry of ≥0.2 whereas the asymmetry required for Level 1 diagnosis in later analysis was found to be 0.1. In individuals with VCDR asymmetry between 0.1 and 0.2, the diagnosis of glaucoma was based on the presence of glaucomatous visual fields. The ISGEO classification system is designed to identify moderate, severe glaucoma and those blind from glaucoma and therefore glaucoma 'suspects' and those with early disease may not have been captured. Our estimate is, therefore, a minimal estimate.

One survey team inadvertently used the C-20-1 FDT screening mode in 141 clusters. The C-20-1 mode has greater specificity and is less likely to misclassify a normal field. The C-20-5 has higher sensitivity at detecting early defects at the expense of lower specificity. To overcome the difference visual fields were classified according to the probability of pattern deviation and were equalized for the 2 screening modes.

Having described the high prevalence and distribution of glaucoma in this comprehensive and representative study, we are obliged to recommend a strategy for the prevention blindness and visual impairment from glaucoma in Nigeria and more widely in West Africa. The clinical care of glaucoma in Nigeria remains challenging and we suggest a top-down approach [60].

Conclusion

This nationally representative survey in Nigeria indicates a high prevalence of glaucoma, with ethnic variation, severity at an earlier age and high rates of blindness. The latter is likely to reflect an aggressive natural history as well as lack of awareness of the condition and low levels of treatment. Most glaucoma in Nigeria is POAG with a high proportion of secondary glaucoma being the consequence of procedures for cataract. The findings shed light on the more severe and prevalent disease seen in black communities of the West African diaspora around the world and quantify the enormous challenge of preventing blindness from glaucoma in West Africa and in people of this ethnic origin. Public health control strategies with high quality integrated glaucoma care services will be required to reduce morbidity and blindness.

Abbreviations

AC: anterior chamber; BIO: binocular indirect ophthalmoscopy; CI: confidence interval; FDT: frequency doubling technology; GPZ: geo-political zone; IOP: intraocular pressure; ISGEO: International Society of Geographical and Epidemiological Ophthalmology; MEHRC: Moorfields Eye Hospital Reading Centre; NC: North central; NE: North east; NW: North west; OAG: open-angle glaucoma; PACG: primary angle-closure glaucoma; PDP: pattern deviation plot; POAG: primary open-angle glaucoma; RAPD: relative afferent pupillary defect; SD: standard deviation; SE: South east; SS: South south; SW: South west; TDP: total deviation plot; VA: visual acuity; VCDR: vertical cup:disc ratio; VH: Van Herick's; WHO: World Health Organization.

Competing interests

No conflicting relationship exists for any author.

Authors' contributions

FK developed the study concept and design, carried out acquisition of data, performed the statistical analysis and interpretation of data, drafted the manuscript, obtained funding and is accountable for all aspects of the work. GE carried out acquisition and interpretation of data and revised the manuscript for important intellectual content. MR participated in acquisition and interpretation of data and revised the manuscript for important intellectual content. PS involved in developing the study design, participated in interpretation of data, revised the manuscript for important intellectual content and was involved in the study supervision. RW was involved in developing the study design, participated in the interpretation of data, helped in drafting the manuscript, revised the manuscript for important intellectual content and was involved in the study supervision and coordination. WN was involved in developing the study design, participated in the interpretation of data, revised the manuscript for important intellectual content and was involved in the study supervision and coordination. GM was involved in developing the study concept and design, acquisition and interpretation of data, revised the manuscript for important intellectual content and was involved in the study supervision and coordination. CE was involved in developing the study concept and design, acquisition and interpretation of data, drafting of the manuscript, revised the manuscript for important intellectual content, lead the study supervision and coordination, obtained funding and is accountable for all aspects of the work. All authors read and approved the final version of the manuscript.

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Data availability statement

Data is currently with the authors as work is on-going but will be deposited at the Federal Ministry of Health, Nigeria:
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Chapter 7

Agreement in measurement of optic cup-to-disc ratio with stereo biomicroscope funduscopy and digital image analysis

Results from the Nigeria National Blindness and Visual Impairment Survey

Digital fundus photography

Research paper investigating the agreement between clinical and digital photo VCDR measurements in a subset of participants who had both methods of assessment

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SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Ophthalmic Epidemiology		
When was the work published?	December 2016		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I collected data as part of the survey team. I performed the statistical analysis. I wrote the first draft of the manuscript and prepared subsequent revisions with consideration of comments from co-authors

Student Signature: Kyari **Date:** 21 December 2016

Supervisor Signature: CEGilbert **Date:** 21 December 2016

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Title

Agreement in measurement of optic cup-to-disc ratio with stereo bio-microscope funduscopy and digital image analysis.

Results from The Nigeria National Blindness and Visual Impairment Survey

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Previous presentation

The findings in this paper have been previously presented, in part, at the 23rd ISGEO Congress, London, United Kingdom. September, 2014.

This submission has not been published anywhere previously and it is not simultaneously being considered for any other publication.

Abstract

Purpose:

To determine agreement of estimations of vertical cup-to-disc ratios (VCDR) between clinical stereo-biomicroscopic funduscopy and digital fundus images analysis.

Methods:

Systematic sampling of 1-in-7 from a sample of 13,591 participants aged ≥40 years gave a subsample who were examined in detail. VCDR was estimated clinically by 60D aspheric lens biomicroscopic funduscopy (c-VCDR) and by fundus images (i-VCDR) graded at Moorfields Eye Hospital Reading Centre. Spearman's correlation coefficient, paired t-test and Bland-Altman method to assess limits of agreement (LOA) between the two methods were applied.

Results:

Of 1759 participants in the subsample, 848 participants (48%) who had normal FDT visual fields and data for i-VCDR and c-VCDR in both eyes (n=1696 eyes) were analysed. By absolute difference of VCDR values for each eye, between the two methods, 94% eyes (n=1585) differed by ≤0.2. Mean i-VCDR was 0.381, standard deviation (SD) 0.156; and mean c-VCDR 0.321, SD 0.145. i-VCDRs were significantly larger by a mean difference of 0.061 SD 0.121 (95% confidence interval [95%CI] 0.055-0.066; $p<0.001$). The 95% LOA assessed by the Bland-Altman method were lower limit -0.182 (95%CI -0.192; -0.172) and upper limit 0.303 (95%CI 0.293; 0.313). The interval of the 95% LOA narrowed with higher VCDRs.

Conclusion:

Digital image analysis and clinical assessment are two distinct methods of measurement for VCDR; with larger i-VCDRs in this survey. Applying i-VCDR cut-off values to c-VCDR measurements in the Nigeria Blindness Survey might have underestimated glaucoma prevalence. It is recommended that all participants in glaucoma surveys have VCDR by digital image measurement.

Introduction

Glaucoma is the leading cause of irreversible blindness. It is projected to affect up to 80 million people by the year 2020[1] and 111.8 million in 2040.[2] In population-based surveys, evidence of structural optic disc damage is an essential element in identifying individuals who may have glaucoma. The optic vertical cup-to-disc ratio (VCDR) is one of the ways of determining optic disc structural damage.

For the Nigeria National Blindness and Visual Impairment Survey (hereafter referred to as the Nigeria Blindness Survey)[3] glaucoma classification was according to the ISGEO criteria.[4] The glaucoma-defining VCDR values for the 97.5th (0.7) and 99.5th (0.75) percentiles in the study population[5] were applied, reporting a glaucoma prevalence of 5.02% (95%CI 4.60-5.47) among adults aged 40-years old and above.[6] The i-VCDR grading by Moorfields Eye Hospital Reading Centre (MEHRC) was considered the gold standard; it was objective, quantified with a scale and adjudicated. According to the survey protocol, participants who had good visual acuity of 6/9 or better in both eyes would not have fundus photography except if they were among the 1-in-7 subsample or if they had disc abnormalities suggestive of glaucoma detected by direct ophthalmoscopy. Also, fundus photography was not obtained for all participants. Thus, these i-VCDR cut-off values were also applied to clinically graded VCDR of participants who did not have digital fundus photography with optic disc imaging.

In this report, data from the Nigeria Blindness Survey were analysed to determine the agreement in measurement of i-VCDR and c-VCDR among adults aged $\geq$40 years in a subset of participants who had both methods of assessment i.e. the 1-in-7 subsample. Determining the agreement between the two VCDR measurement methods will potentially inform VCDR measurement in subsequent glaucoma prevalence surveys. It will also enable better interpretation of the results obtained by applying the i-VCDR defining percentile values to the whole dataset for glaucoma classification in the National Blindness Survey.

Methods

Details of all the methods used in the Nigeria Blindness Survey,[3] a report on the defining values for glaucoma in prevalence surveys in Nigeria[5] as well as the prevalence and types of glaucoma in Nigeria have been published.[6]

Study design, data collection and clinical assessment

The sample size calculation and sampling strategy for the Nigeria Blindness Survey gave a nationally representative sample of 15,375 persons aged 40 years and above in 310 clusters across the country. Multi-stage sampling using probability-proportional-to-size methods were used to select the study population. A further systematic sampling of 1-in-7 participants registered at the examination centre was done. All participants were invited to a temporary clinic-type set up for examination. Data were collected by two teams, each comprising of two ophthalmologists, one optometrist and two ophthalmic nurses. The ophthalmologists received further training in survey protocols and standardising VCDR measurement.

Systematic sampling of 1-in-7 from a sample of 13,591 participants aged ≥40 years gave a subsample who were examined in detail, including visual field assessment with a Humphrey FDT visual field analyzer (Carl Zeiss Meditec AG Jena Germany).

The first ophthalmologist performed undilated direct funduscopy. Detailed eye examination performed by the second ophthalmologist included slit-lamp biomicroscopy (Zeiss SL 115 Classic Slit Lamp, Carl Zeiss Meditec AG Jena Germany) and dilated retinal examination and optic disc assessment using 60D aspheric condensing lens (Volk). VCDR was estimated clinically (c-VCDR) by determining the rim of the optic disc and estimating the cup size in the vertical meridian and calculating the spatial ratio between the optic cup and the optic disc.

Participants also had digital retinal photography (Zeiss Visucam Lite Desk Top Fundus Camera, Carl Zeiss Meditec AG Jena Germany) through a dilated pupil focused mid-point between the macular and optic nerve head displaying a field of 45 degrees showing both the macula and the optic disc in the observed field. Images were graded independently by the Moorfields Eye Hospital Reading Centre (MEHRC). Images were viewed "full screen" on either a 24-inch Eizo S2433W monitor calibrated using a Datacolor Spyder2 calibrator or on a 24-inch widescreen Dell 2407WFP LCD monitor calibrated using a Gretag Macbeth Eye-One Display 2 calibrator. After determining image quality and clarity, the scleral rim was identified and the boundaries of the disc and the cup were identified. One successful measurement was performed per eye, along the vertical meridian, in Adobe Photoshop (version 7) using the measurement tool, resulting in a cup and a disc diameter value in pixels, along the same plane, the division of the two values producing the i-VCDR which was recorded to the nearest 0.05. Primary grading was performed by the 1st reader (FS), and a 2nd reader (NP) and inconclusive cases were adjudicated by a 3rd reader (TP).

Inter-observer agreement assessments were conducted for ophthalmologists on c-VCDR measurement during the training sessions and at intervals during fieldwork. There was one clinical ophthalmologist in each of the two teams throughout the survey. For i-VCDR grading, inter-observer agreement between the 1st and 2nd readers was assessed. Kappa statistics for inter-observer error were calculated.

Ethics

Ethical approval was obtained from the Ethics Committee of the London School of Hygiene and Tropical Medicine (LSHTM), UK and the Nigeria National Health Research and Ethics Committee (NHREC). Oral informed consent was obtained from participants. The study adhered to the tenets of the declaration of Helsinki. Persons with medical or eye conditions needing further assessment and treatment were referred to the nearest healthcare facility.

Data analysis

Statistical analysis was performed using Stata/IC 14.0 (Stata Corp, College Station, TX). Included in the analysis were both eyes of the 848 participants in whom both eyes had VCDR grading by the two methods (slit-lamp biomicroscopic funduscopy with 60D aspheric lens and digital fundus photography image analysis), normal FDT visual fields and no detected ocular pathology.

For kappa analysis, ophthalmologists' clinical measurement of VCDR within 0.1 in one session was assessed; and image grading within 0.2 obtained by the two primary readers was assessed.

Frequency distribution of the absolute difference between the VCDR values in each eye was determined. The frequency distributions of c-VCDR and i-VCDR were determined and compared; and the Shapiro-Wilk test of normality was applied. The association between the two methods of measurement was calculated and expressed as the Spearman's rank-order correlation coefficient.

Paired t-test was applied for comparison of means to investigate the presence of any systematic (fixed) bias.

Bland-Altman method to assess 95% limits of agreement (LOA) between the two methods was applied.[7-9] To assess agreement on the Bland-Altman plot, the y-axis was the difference between the two measurement methods (i-VCDR minus c-VCDR), i.e. the amount of disagreement, plotted against the x-axis, the mean of the two measurements. The LOA were the mean differences $\underline{+}$ 2 standard deviation of the differences. The 95% confidence intervals for the upper and lower LOA were calculated. The difference between the two measurement methods was regressed on the average of the two measurements and the slope of least-squares regression with the regression-based 95% LOA were determined. The slope of the least squares regression line was tested if it significantly differed from zero, to investigate the presence of any proportional bias. The adjusted R-squared was calculated by linear regression analysis.

The Bland-Altman method was also applied to the data where c-VCDR was $\geq$0.6 and a quadratic regression line was determined.

Results

The kappa for inter-observer agreement for ophthalmologists' clinical measurement of VCDR within 0.1 was κ=0.86 (almost perfect agreement), calculated for one assessment session for 85 eyes. For the image VCDR grading at MEHRC, the overall inter-observer agreement between two graders for 847 eyes was 99.7% and the kappa for $\leq$0.2 difference between graders was κ=0.50 (moderate agreement).

Both eyes of 848 participants (n=1696) were included in the analysis. All eyes had data for VCDR obtained by the two methods of measurement. The clinical estimates recorded a zero (0) VCDR in 63 eyes (3.7%); and were recorded in 0.1 difference steps. The image grading was recorded in 0.05 steps in 103 eyes (6.1%) (**Figure 1**).

Frequency distribution of the absolute difference of VCDR values for each eye, between the two methods showed that 75% eyes (n=1278) differed by $\leq$0.1, and 94% eyes (n=1585) differed by $\leq$0.2.

The Shapiro-Wilk test for normality of data showed that the i-VCDR had a high value of W (0.994) but p<0.001. Thus the distribution of values for i-VCDR in this sample did not follow a normal distribution. The distribution of values for c-VCDR followed a normal distribution (W=998, p=0.10).

The Spearman's rank-order correlation coefficient showed a strong positive correlation between i-VCDR and c-VCDR which was statistically significant (r_s=0.67, p<0.001).

The mean VCDR differed significantly between the i-VCDR, 0.381 standard deviation (SD) 0.156 and the c-VCDR, 0.321 SD 0.145. The difference in the means was 0.061 (95%CI 0.055 – 0.066), SD 0.121, p<0.001 and suggestive of a systematic (fixed) bias. Where the c-VCDR was $\geq$0.6 (n=98) the difference in the two means was 0.022 (95%CI 0.002-0.042), SD 0.101; p=0.03.

The Bland-Altman plot in Figure 2 shows agreement between the two methods of estimating VCDR where the difference between the two measurement methods was plotted against the average of the two measurements, which is assumed to be the best estimate of the true value. The line of no difference (a; solid green line) indicates where there is no difference between the two methods of measurement at this level. Most of the points are above this line, indicating that measurements of i-VCDR were higher than c-VCDR with an average discrepancy bias of 0.061, indicated as a solid red line (b). The 95% LOA are indicated by the two solid horizontal black lines (c) which demarcate the upper LOA 0.303 (95%CI 0.293 to 0.313) and the lower LOA -0.182 (95%CI -0.192 to -0.172). Figure 2 also shows the least squares regression line indicated by the red dash line (d) with regression-based 95% LOA (e; dash-3dot lines). The trend in the plot showed that the interval between the upper and lower LOA narrowed with higher VCDR values showing fewer data points and indicating that the differences between the two measurements became smaller for higher average VCDR values. The least squares linear regression line (d; red dash line) significantly differed from zero ($p<0.001$), indicating the existence of proportional bias. The existence of proportional bias implies that the two methods of VCDR measurement did not agree equally through the range of measurements.

Further, in eyes with c-VCDR$\geq$0.6 (n=98) the quadratic model (**Figure 3**), appeared to fit the data better than a linear model with the quadratic regression line (d; red dash line) trending towards the line of no difference (a; solid green line) as the average VCDRs increase.

Discussion

In investigating the difference between the two methods of measurement of VCDR by clinical slit-lamp biomicroscopic funduscopy with 60D aspheric lens and by digital fundus photography image grading, the use of Bland-Altman method of assessment[7-9] determines how closely the two methods agreed. The discrepancy between the two methods was clinically substantial and showed that they were two distinct methods of measurement of VCDR with a statistically significant average discrepancy of 0.061. With higher c-VCDRs, the average discrepancy was less (0.022). This may mean that when the disc changes are obvious, the detection and measure would be easier and more similar for both methods. Digital image analysis gave larger VCDRs than clinical assessment. We acknowledge this difference, thus the application of image VCDRs glaucoma-defining percentile values to the whole Nigeria Blindness Survey data might have underestimated the prevalence of glaucoma in the population.

The advantages of using digital image grading of the VCDR were that the disc images, under the survey conditions, could be captured and kept as records, which could be reviewed objectively and quantified with a scale. The images could also be used for follow-up. However, the disadvantages were that the fundus camera did not take stereoscopic images so monocular clues were used to determine cup and disc boundaries; and the angle of projection might affect the spatial measurement of disc parameters. Whereas with the 60D aspheric lens, stereoscopic images were viewed and assessed but a measurement graticule was not used; and the disc assessments were not documented with hand-drawings on a template, thus it would be difficult to review afterwards or adjudicate.

The Bland-Altman method to assess LOA has been applied to various methods of measuring VCDR and the results vary. Jayasundera[10] and Durmus,[11] in their respective studies, found poor agreement between stereoscopic photographs, clinical assessment, HRT and digital stereoscopic optic disc camera which was worse for small discs and smaller cups.[10] The Rotterdam study also showed that semi-automated VCDR measurements were larger than ophthalmoscopic estimates with a moderate correlation.[12] Perera compared clinical measurement of VCDR (mean 0.40±0.12) using an eyepiece graticule with HRT (mean 0.37±0.21) and with OCT (mean 0.50±0.14) and found lack of agreement

($p<0.001$), with OCT tending to overestimate VCDR and HRT tending to underestimate values.[13]

Limitations of this study are that it was a retrospective analysis and a graticule was not incorporated in the clinical VCDR measurement. A 0.01mm graticule might have increased the accuracy of clinical measurement and also improved inter-observer agreement.[14] Regarding image quality, lack of centration of the optic disc in the image could have contributed to differences due to magnification and positioning. An algorithm for measurement which takes into account the magnification factor and the actual size in micrometre of one pixel used directly on the images with the participant still available for re-examination has been found to be useful in both population-based measurement and clinical practice.[15]

Based on the differences between the two methods, the use of optic disc imaging/photography with digital image analysis for measurement of VCDR is recommended in glaucoma prevalence survey for all participants. This will provide uniformity and objective evaluation of VCDR and comparable glaucoma prevalence estimates.

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Figures legend

Figure 1. The frequency distribution of values for image VCDR and clinical VCDR

Figure 2. Bland-Altman plot comparing VCDR measured by clinical slit-lamp biomicroscopy funduscopy and by fundus photography image grading

Figure 3. Bland-Altman plot comparing VCDR measured by clinical slit-lamp biomicroscopy funduscopy and by fundus photography image grading if c-VCDR ≥0.6

Figure 1. The frequency distribution of values for image VCDR and clinical VCDR

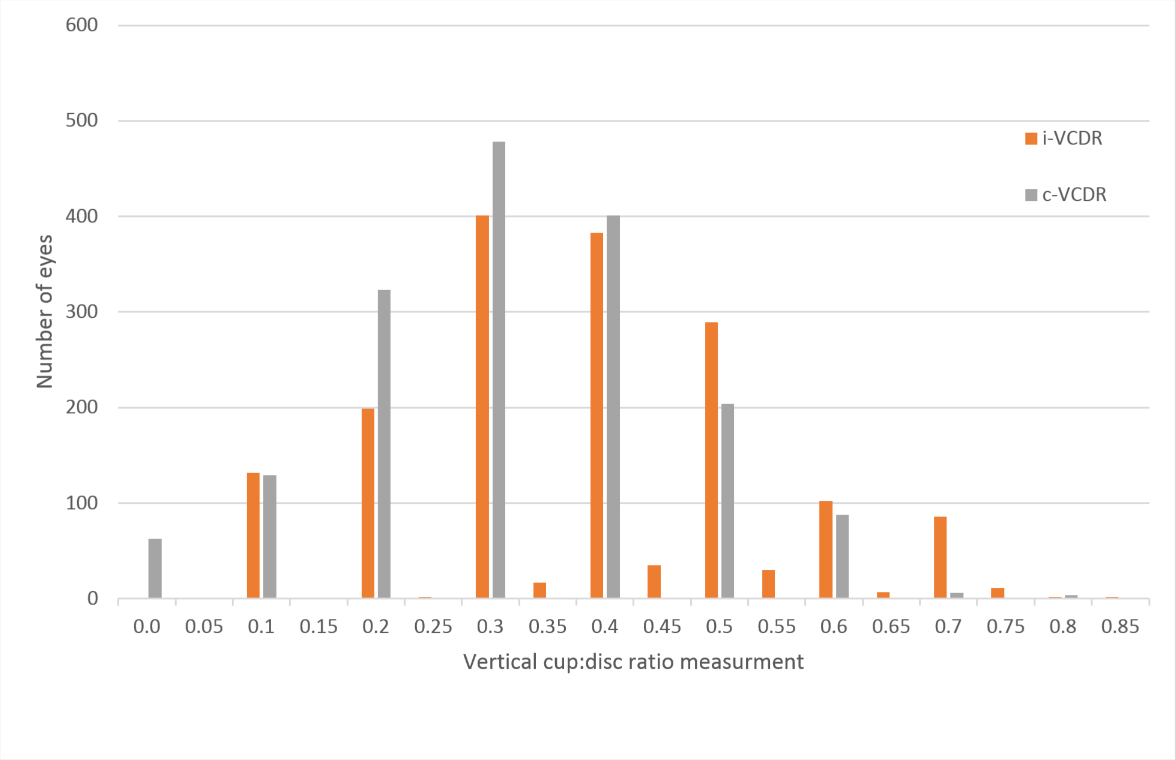
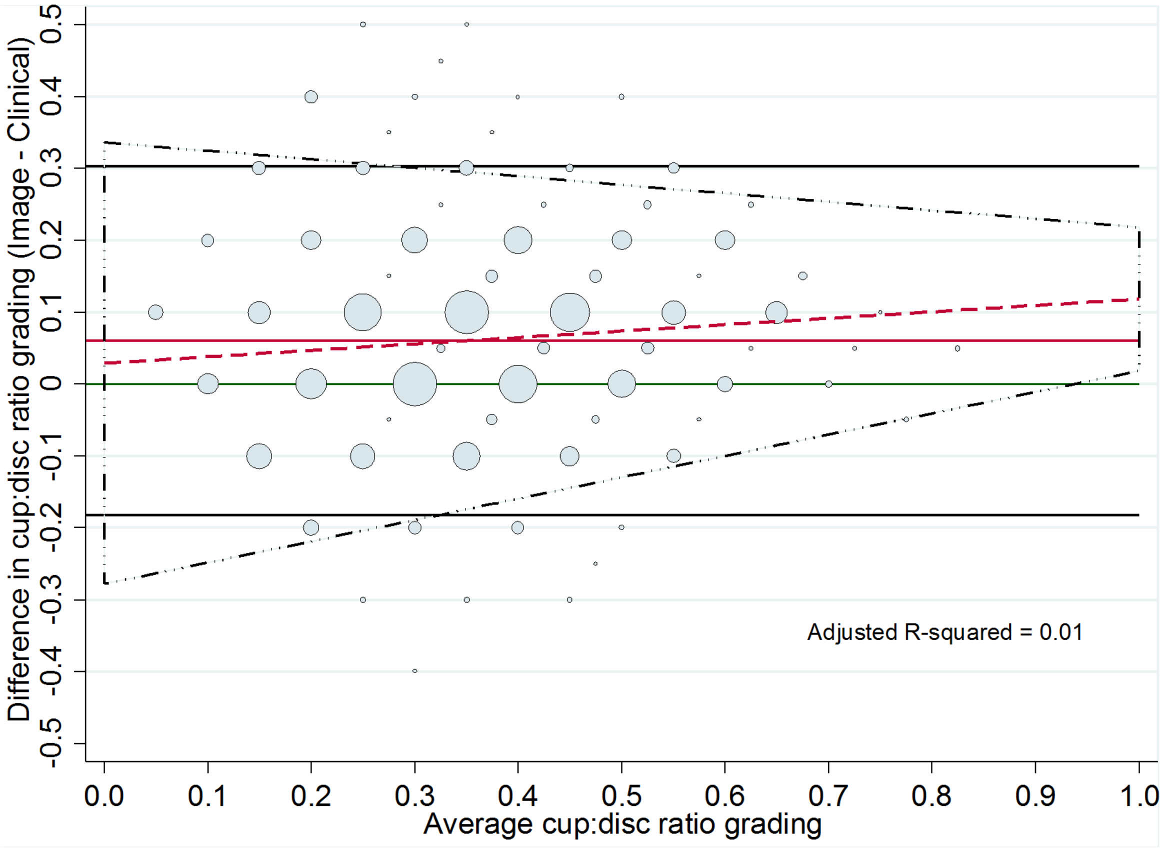


Figure 2. Bland-Altman plot comparing VCDR measured by clinical slit-lamp biomicroscopy funduscopy and by fundus photography image grading



Lines shown indicate:

a) ______________ Solid green line is the line of no difference at zero.

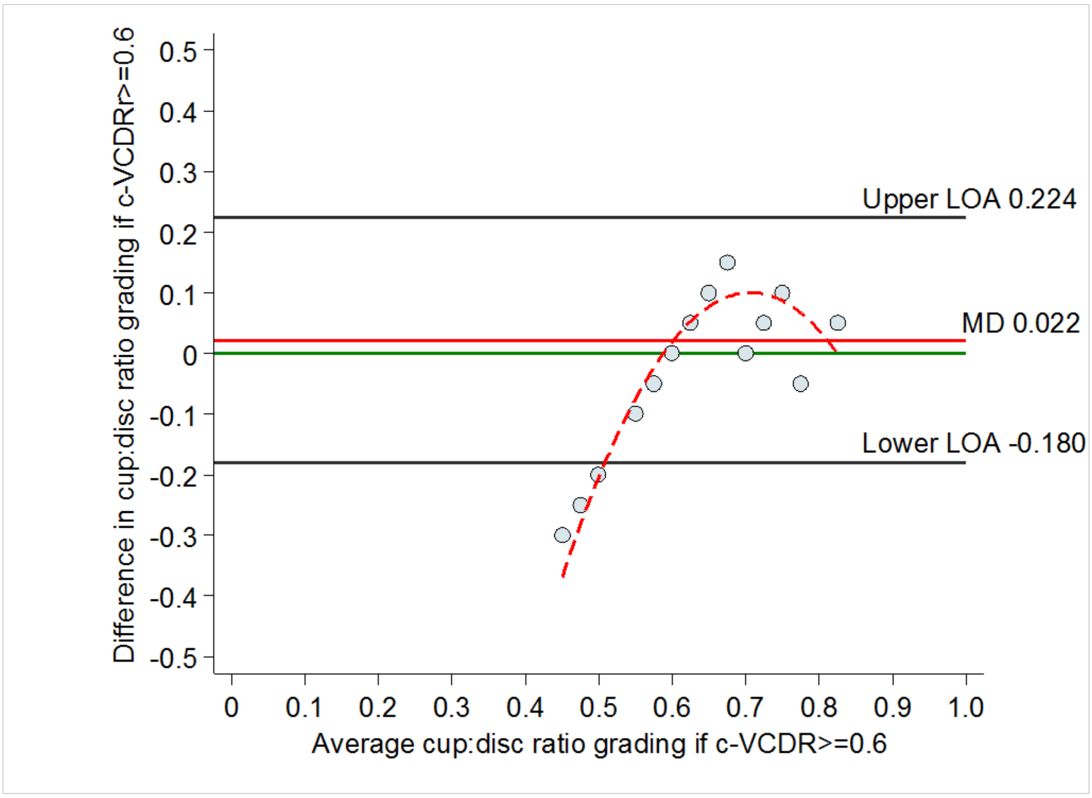
b) ______________ Solid red line is the mean difference (0.061)

c) ______________ Solid horizontal black lines demarcate the
upper limit of agreement (Mean + 2SD) 0.303; and
lower limit of agreement (Mean – 2SD) -.182

d) -------------- Red dash line is the slope of least-squares regression for the difference between the two measurements on the average of the 2 measurements.

e) _..._..._ Dash-3dot lines are the regression-based 95% limits of agreement

Figure 3. Bland-Altman plot comparing VCDR measured by clinical slit-lamp biomicroscopy funduscopy and by fundus photography image grading if c-VCDR≥0.6



Lines shown indicate:

a) ____________ Solid green line is the line of no difference at zero.
b) ____________ Solid red line is the mean difference (0.022)
c) ____________ Solid horizontal black lines demarcate the
upper limit of agreement (Mean + 2SD) 0.224; and
lower limit of agreement (Mean – 2SD) -0.180
d) -------------- Red dash line is the quadratic regression for the difference between the two measurements on the average of the two measurements.

c-VCDR = clinical vertical cup:disc ratio; LOA = limit of agreement; MD = mean difference; SD = standard deviation.

Chapter 8

Risk factors for open-angle glaucoma in Nigeria

Results from the Nigeria National Blindness and Visual Impairment Survey

Some information in this paper was presented, in part, as a poster at the Association of Research in Vision and Ophthalmology conference (ARVO) 2014, Orlando, USA

Research paper exploring the risk factors for open-angle glaucoma

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SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	BMC Ophthalmology		
When was the work published?	June 2016		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	Yes, *see Appendix 7c*	Was the work subject to academic peer review?	Yes

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I collected data as part of the survey team. I developed the glaucoma diagnosis algorithm. I performed the statistical analyses. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors.

Student Signature: Kyari **Date:** 28 June 2016

Supervisor Signature: CEGilbert **Date:** 30 June 2016

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RESEARCH ARTICLE

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Risk factors for open-angle glaucoma in Nigeria: results from the Nigeria National Blindness and Visual Impairment Survey

Fatima Kyari[1,2*], Mohammed M. Abdull[1,3], Richard Wormald[1,4], Jennifer R. Evans[1], Winifred Nolan[4], Gudlavelleti V. S. Murthy[1,5], Clare E. Gilbert[1] and On behalf of the Nigeria National Blindness and Visual Impairment Study Group

Abstract

Background: The glaucoma-specific blindness prevalence in Nigeria (0.7 %, 95 % CI 0.6–0.9 %) among those aged ≥40 years is one of the highest ever reported. This study determined the risk factors for open-angle glaucoma (OAG) in adults examined in the Nigeria National Blindness and Visual Impairment Survey.

Methods: A nationally representative sample of 13,591 people aged ≥40 years in 305 clusters in Nigeria were examined (response rate 90.4 %) between January 2005 to June 2007. Everyone had logMAR visual acuity measurement, Frequency Doubling Technology (FDT) visual field testing, autorefraction, A-scan biometry and optic disc assessment. Full ocular examination ($n = 6397$), included Goldmann applanation tonometry. Values for defining glaucoma using International Society of Geographical and Epidemiological Ophthalmology criteria were derived from the study population. Disc images were graded by Moorfields Eye Hospital Reading Centre. Socio-demographic factors (age, gender, ethnicity, literacy and place of residence), ocular parameters (intraocular pressure [IOP], axial length and mean ocular perfusion pressure [MOPP]) and systemic parameters (blood pressure, blood glucose and body mass index [BMI]) were assessed for association with OAG.

Results: Thirteen thousand eighty-one (96 %) of 13,591 participants had vertical cup:disc ratio measured in at least one eye. 682 eyes of 462 participants were classified as OAG, with 12,738 controls. In univariate analyses the following were associated with OAG: increasing age, male gender, Igbo and Yoruba ethnic groups, illiteracy, longer axial length, higher IOP, lower MOPP, greater severity of hypertension and low BMI (underweight). In multivariate analysis, increasing age (odds ratio [OR] 1.04, 95 % CI 1.03–1.05), higher IOP (OR 1.22, 95 % CI 1.18–1.25) and Igbo ethnicity (OR 1.73, 95 % CI 1.18–2.56) were independent risk factors for OAG.

Conclusion: Case detection strategies for OAG should be improved for those aged ≥40 years and for ethnic groups most at risk as a public health intervention.

Keywords: Open-angle glaucoma, Risk factors, Ethnicity, Nigeria

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Background

In 2013 it was estimated that there were 64.3 million people aged 40–80 years with glaucoma worldwide, projected to increase to 76.0 million by the year 2020 and 111.8 million in 2040 [1]. Open-angle glaucoma (OAG) is the most prevalent type of glaucoma in Africa [1–6] and a leading cause of blindness and visual impairment [2, 7]. The glaucoma-specific blindness prevalence in Nigeria (0.7 %, 95 % confidence interval [CI] 0.6–0.9 %) among those aged 40 years and above is one of the highest ever reported [8], and glaucoma is the second-leading cause of blindness after cataract [8]. The all glaucoma prevalence in Nigeria in this age-group was 5.02 % (95 % CI 4.60–5.47 %), with 86 % being OAG based on gonioscopy. An estimated 1.2 million adults in Nigeria had glaucoma in 2012 [9].

There are some similarities in the epidemiology of OAG in sub-Saharan African and Caribbean populations. An interesting aspect of the Barbadian history is that a significant portion of the population was derived from the Bight of Biafra (also known as Bight of Bonny) in southeastern Nigeria; and about 44 % of enslaved Africans taken to Barbados during the 18th century were said to be mainly of Igbo origin [10]. Studies of risk factors for OAG in sub-Saharan Africa and African-derived black populations have reported that increasing age [3–6, 11–13] and higher intra-ocular pressures (IOP) [3, 4, 12, 14] are consistent and important risk factors. Although not always observed, men have a higher prevalence of glaucoma [4, 5, 12, 15]. A consistent finding is a higher prevalence of OAG in blacks compared to whites in populations where the two racial groups were studied [11, 13, 15]. The prevalence of glaucoma was higher in those with darker skin and of African birth [13], which suggest possible influence of environmental factors and inter-ethnic variation in the prevalence and risk of OAG within black populations, mediated by genetic factors. A higher prevalence of OAG in the urban population of Chennai compared to the rural population suggest a possible influence of lifestyle differences and non-communicable diseases such as hypertension and diabetes which are also more prevalent in the urban population [16]. Very few studies have explored other socio-demographic and systemic risk factors.

The Nigeria National Blindness and Visual Impairment Survey (hereafter referred to as the Nigeria Blindness Survey) is one of the largest population-based survey ever undertaken in Africa [17]. The present paper analysed data from the Nigeria Blindness Survey to explore risk factors for OAG among adults aged ≥40 years. Factors other than age and IOP were assessed. Identifying population groups most at risk, such as ethnic groups, will aid in planning appropriate control strategies and enhance the development of care-pathways to prevent visual loss from glaucoma. It is envisaged that these results will also be relevant to other countries in sub-Saharan Africa and for African-derived black populations.

Methods

Details of all the methods used in the Nigeria Blindness Survey have been published [17] as well as data on the prevalence [7] and causes of visual impairment and blindness [8] and the prevalence and types of glaucoma in Nigeria [9].

Study design

The sample size calculation and sampling strategy for the Nigeria Blindness Survey gave a nationally representative sample of 15,375 persons aged 40 years and above in 310 clusters across the country. The sample size was also adequate for precise estimates of glaucoma prevalence and was adequately powered for risk factor analysis for OAG.

Multi-stage sampling using probability proportional to size methods was used to select the study population. Clinical data were collected by two teams, each comprising two ophthalmologists, one optometrist and two ophthalmic nurses.

Data collection

All participants were invited to a temporary clinic for examination. Relevant personal and demographic details and examination findings were recorded.

The examination flow chart (Fig. 1; adapted [17]) indicates the data collected by the team members. All participants had presenting and best-corrected visual acuity (VA) measured with a reduced logMAR tumbling E-chart, automated refraction and keratometry (Takagi ARKM-100, Takagi Seiko, Japan), frequency doubling technology (FDT) visual function testing (Carl Zeiss Meditec AG Jena Germany) and ultrasound A-scan biometry (Bioline Biometer OPTIKON 2000 S.p.A Roma, Italy). All participants had basic eye examination performed by the first ophthalmologist, and detailed ocular examination was performed by the second ophthalmologist: in those with VA of worse than 20/40 in one or both eyes; vertical cup:disc ratio (VCDR) ≥0.6 in one or both eyes or VCDR asymmetry of ≥0.2, or any retinal abnormality seen on undilated fundoscopy [17]. In addition, a subsample of 1-in-7 participants who also had the detailed examination regardless of their VA had a random blood glucose (RBG) test (OneTouch Ultra blood glucose meter, LifeScan UK).

Risk factors assessment and classification

There were five socio-demographic ‘person’ factors (age, gender, ethnic group, literacy and place of residence), six

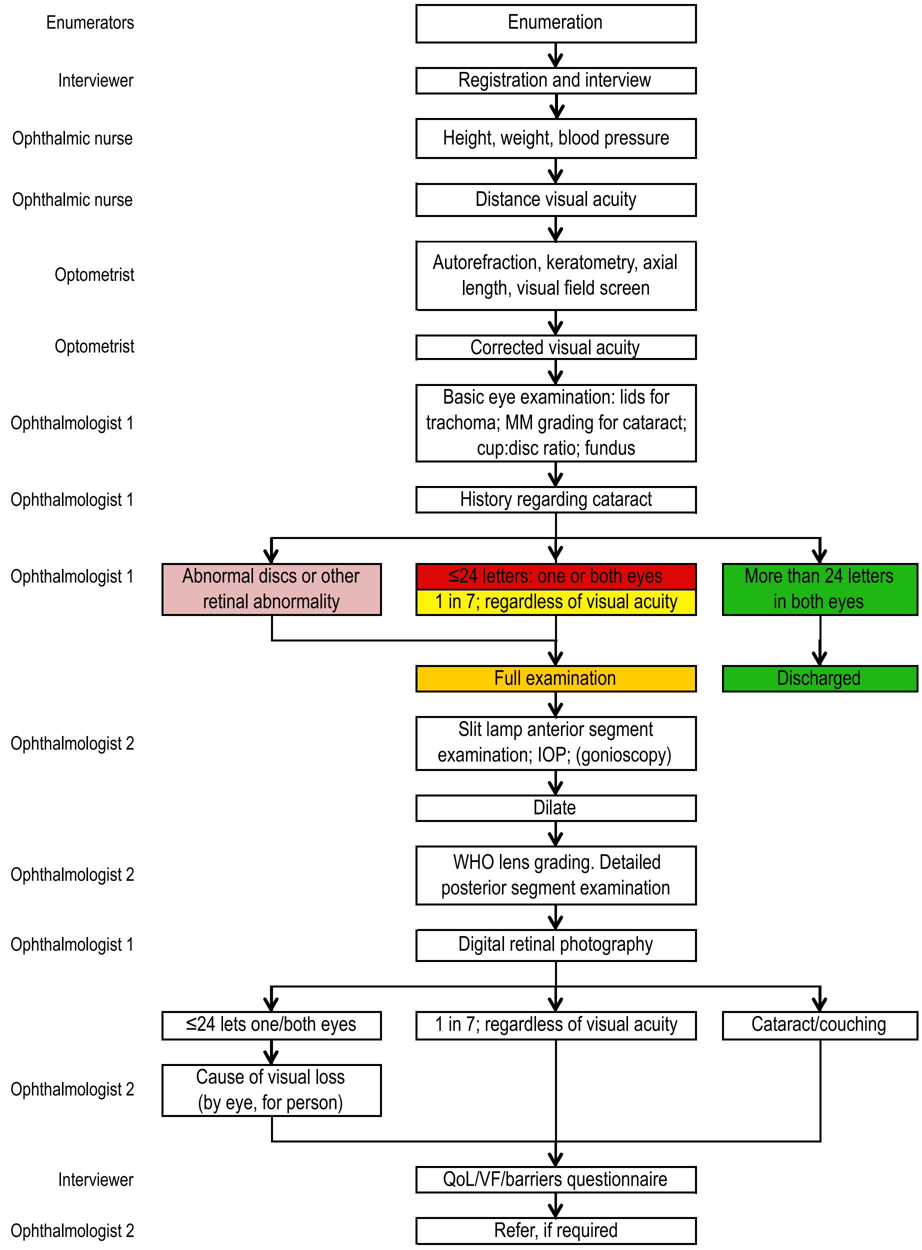


Fig. 1 The Nigeria Blindness Survey examination flow chart

biophysical ‘person’ factors (presence of hypertension, severity of hypertension, systolic blood pressure [SBP], diastolic blood pressure [DBP], RBG and body mass index [BMI]); and three ‘ocular’ factors (axial length, IOP and mean ocular perfusion pressure [MOPP]). Age was analysed as a continuous variable and gender as a binary variable. Participants were asked about their ability to read and/or write and their ethnic group. Literacy was classified as ability to read and write or not at all and analysed as a binary variable. The geographical origins of some of the major ethnic groups are shown in Fig. 2. The Ibibio and Ijaw are from the southern Niger delta region, the Igbos and Urhobos are from the southeastern equatorial region and the Hausa, Fulani and Kanuri are from the northern savannah region. Ethnic groups with ≥200 participants (Hausa, Yoruba, Igbo, Fulani, Kanuri, Tiv, Ijaw, Urhobo, Ibibio and Nupe) were categorised and analysed separately, and the smaller ethnic groups were combined into an ‘others’ category. Urban place of residence was defined as a settlement of more than 20,000 people.

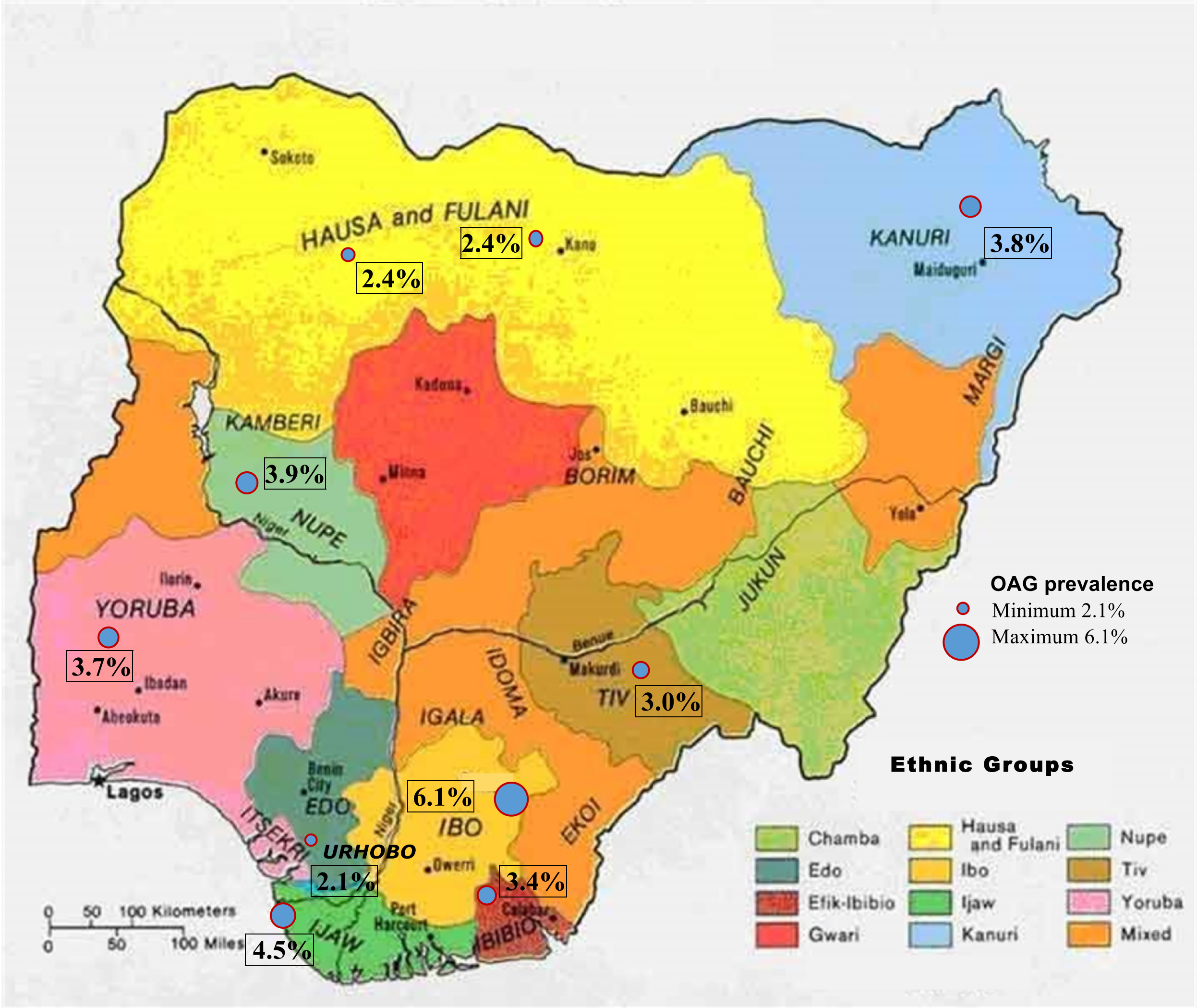


Fig. 2 Geographical origins of ethnic groups and their open-angle glaucoma prevalence. Adapted from Map of the ethno-linguistic groups of Nigeria. Source: University of Texas Libraries; obtained from https://commons.wikimedia.org/wiki/File:Nigeria_linguistic_1979.jpg

Blood pressure (BP) was recorded three times with BP Omron wrist instrument (Omron Healthcare Ltd, Milton Keynes, England) after resting for at least 10 min [18]. Average values were used for analysis. Hypertension was defined as BP ≥140/90 mmHg and severity was categorised using World Health Organization (WHO) categories: stage 1 for systolic/diastolic BP of ≥140/90 mmHg, stage 2 ≥ 160/100 mmHg and stage 3 ≥ 180/110 mmHg [19]. SBP and DBP were analysed as continuous variables. RBG was grouped as less than 11.1 mmol/L or ≥11.1 mmol/L [20]. Height was measured to the nearest tenth of a centimeter and weight was measured to the nearest 100 g using standard equipment. BMI was calculated by dividing body weight (kg) by height (m) squared and categorised according to the international classification for adults i.e., underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obese (≥30.0 kg/m^2) [21].

Axial length was measured by contact ultrasound A-scan biometry. IOP was measured using one Goldmann applanation tonometer in each of the two teams by the second ophthalmologist, using standard methods. To explore the association of vascular perfusion and OAG, the MOPP was calculated as $^{2}/_{3}$[DBP + $^{1}/_{3}$ (SBP-DBP)-IOP] [22]. Axial length, IOP and MOPP were analysed as continuous variables.

A person was classified as having glaucoma if one or both eyes had glaucoma. The diagnosis of glaucoma was based on the International Society for Geographical and Epidemiological Ophthalmology (ISGEO) criteria with defining values obtained from a subsample of this study population [23]: VCDR ≥0.7 or VCDR asymmetry ≥0.1

(97.5th percentile) with evidence of glaucomatous visual function deficit; or VCDR ≥0.75 or VCDR asymmetry ≥0.2 (99.5th percentile) when visual fields results were not available; or IOP ≥28 mmHg (99.5th percentile) ± VA worse than 20/400 or known glaucoma on treatment; or if there was relative afferent pupillary defect (RAPD) associated with high IOP and/or corneal edema. The Van Herick's anterior chamber (AC) angle estimation was performed on the slit-lamp with a narrow slit of light projected on the peripheral cornea, and was based on the relationship between the corneal slit image on the corneal surface and the AC depth. Grades 3 and 4 infer open angles and angle-closure is unlikely. The validity of the Van Herick's method for the estimation of the AC angle to correctly identify grades 3–4 as being open angles was assessed in comparison to identification of open angles by gonioscopy. Eyes with glaucoma were classified as OAG based on open-angles seen on gonioscopy or Van Herick's grades 3–4 in those who did not have gonioscopy.

Data for all participants classified as OAG were compared to those of the control group in analysis. Sociodemographic, ocular and biophysical factors were analysed for associations with OAG. The control group consisted of all other participants without OAG after excluding glaucoma eyes that did not have gonioscopy or Van Herick's test findings and those with other types of glaucoma, and phthisical eyes. The algorithm for selection of OAG cases and the control group is shown in Fig. 1.

Statistical analysis was performed using Stata/IC 13.0 (Stata Corp, College Station, TX).

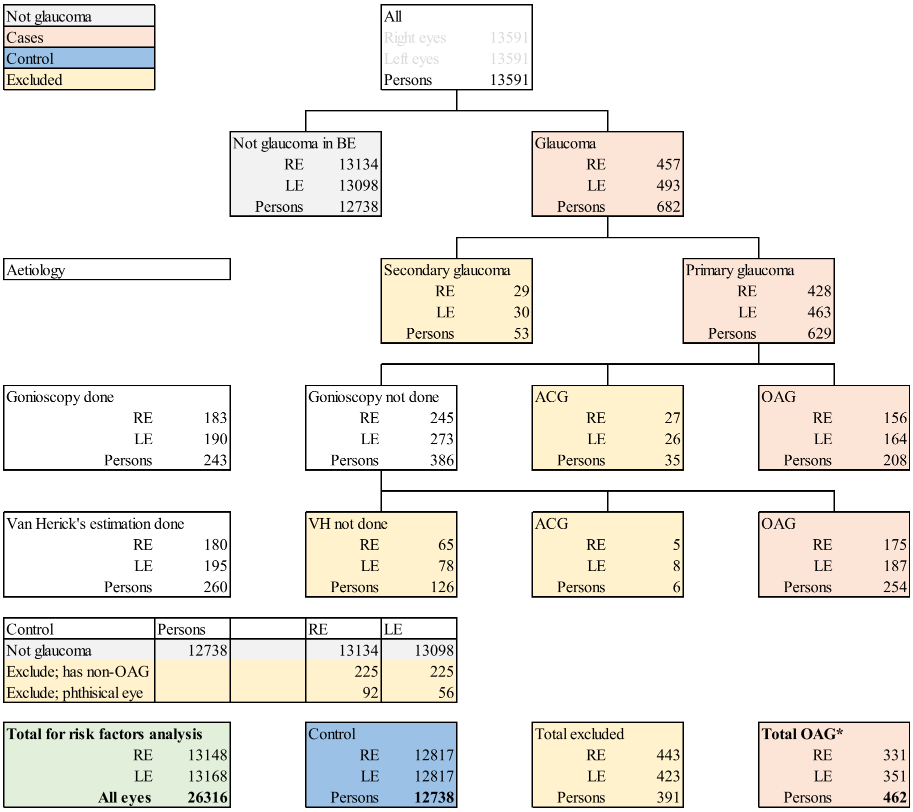
We examined the association between OAG and each risk factor separately and report odds ratios with 95 % confidence intervals (CI). We used logistic regression to assess the independent effect of each risk factor on OAG and report adjusted odds ratios and 95 % CI intervals. BMI was also adjusted for gender. The following variables were included in the multivariable model: age, gender, ethnic group, literacy, rural/urban residence, BP, BMI, ocular axial length, IOP and MOPP. For ocular factors, the analysis took account of within-person correlation using robust standard errors. Possible extra variation introduced by the cluster sampling strategy was also considered but it did not impact the results.

Results

A summary of completeness of data for the Nigeria Blindness Survey has been reported: for participants undergoing full examination (6397), 88 % had IOP measurement with Goldmann applanation tonometer in at least one eye [9]. In the Nigeria Blindness Survey, 950/27,182 (3.50 %) eyes of 682/13,591 (5.02 %) participants had glaucoma according to the ISGEO criteria, of which 320 eyes of 208 persons were classified as OAG by gonioscopy. 375 eyes had Van Herick's AC angle estimation but did not undergo gonioscopy. In eyes with both values, Grades 3 and 4 Van Herick's AC angle estimation had a 99.1 % sensitivity and 93 % positive predictive value in identifying open angles by gonioscopy. Thus, an additional 362 eyes of 254 persons were included as OAG cases as they had grades 3 or 4 Van Herick's estimation. Hence, 462 persons (682 eyes with OAG) were included in the analysis as OAG while 12,738 persons were classified as controls (without OAG) and 391 participants were excluded (Fig. 3).

The OAG group was older and more likely to be male (Table 1). The mean age ± standard deviation (SD) of participants with OAG was significantly higher than that of controls (66.2 ± 12.3 years Vs 55.4 ± 12.1 years, $p < 0.001$). Men with OAG were significantly older (mean age 67.6 years ±12.7) than women with OAG (mean age 64.8 years ±11.8; $p = 0.02$). The OAG group also had a higher proportion of participants that were of the Yoruba or Igbo ethnic group, illiterate and with hypertension and low BMI (underweight). After adjusting BMI for gender, the odds of OAG was higher in underweight women (OR 1.84, 95%CI 1.27–2.68; $p = 0.001$) but not after adjusting for age or for age and IOP. The mean ± SD IOP was higher in eyes with OAG (22 ± 11 mmHg) than in eyes without OAG (14 ± 4 mmHg, $p < 0.001$). Similarly, the mean ocular axial length was longer in eyes with OAG (22.8 ± 1.09 mm) than in those without OAG (22.6 ± 0.97 mm, $p = 0.001$).

In univariate analysis, increasing age was positively associated with OAG (Odds ratio [OR] 1.06, 95 % CI 1.06–1.07; $p < 0.001$), as was being male (OR 1.29, 95 % CI 1.06–1.57; $p = 0.01$) (Table 2). There was 6 % higher odds of OAG with each increasing year of age. The following factors were also positively associated with OAG: Igbo and Yoruba ethnic groups, being illiterate, any hypertension and greater severity of hypertension, low BMI (underweight), longer ocular axial length, higher IOP and lower MOPP (Table 2). When adjusted for myopia, axial length remained significantly associated with OAG (OR 1.13, 95 % CI 1.02–1.25; $p = 0.03$). In multivariate logistic regression analyses, increasing age, higher IOP and Igbo ethnic group were identified as independent risk factors for OAG. The ethnic group-specific prevalence of OAG for the analysed ethnic groups are shown in Fig. 2. The Urhobo had the lowest odds of OAG (OR 0.69, 95 % CI 0.24–1.97), while the Kanuri (OR 1.81, 95 % CI 0.90–3.63; $p = 0.10$) and Igbo (OR 1.73, 95 % CI 1.18–2.56; $p = 0.01$), the highest. The Igbo ethnic group had a 73 % higher odds of OAG than the Hausa (reference group) (Table 2); and when adjusted for gender, Igbo men were 2.5 times more likely to have OAG than Hausa men (OR 2.54, 95 % CI 1,50–4.30; $p = 0.001$).



BE = both eyes; RE = right eye; LE = left eye; ACG = angle-closure glaucoma; OAG = open-angle glaucoma; VH = Van Herick's anterior chamber angle estimation; * = participants have OAG in one or both eyes

Fig. 3 Algorithm for selection of open-angle glaucoma cases and control

Systemic hypertension ($BP \geq 140/90$ mmHg) was also associated with OAG, with moderate and severe hypertension having stronger and significant association with OAG in univariate analysis. After adjusting for age, IOP and other potential risk factors in a multivariable model, mildly elevated BP (stage 1) was protective of OAG compared to participants without hypertension but this was not statistically significant (OR 0.87, $p = 0.52$). There was a strong association between lower MOPP and OAG ($p < 0.001$) in univariate analysis which did not persist after adjusting for age, IOP and other factors.

In univariate analysis, lower BMI was associated with 60 % greater odds of OAG ($p = 0.001$) and the odds decreased with increasing BMI. However, in the adjusted model, BMI was not statistically significant.

Discussion

We report results of the first cross-sectional study of risk factors for OAG in sub-Saharan Africa in a large population-based, nationally representative survey in Nigeria. We did not explore the risk factors for angle-closure glaucoma, as the numbers were too few. Older age and higher IOP were independent risk factors for OAG. Additionally, an important and new finding was that the Igbo ethnicity was an independent risk factor associated with OAG, especially in men.

Significant inter-racial variation between White, Asian and Black populations has been described [11, 13, 15, 24] with the prevalence and risks of OAG being higher in Blacks. However, studies in smaller population groups in sub-Saharan Africa have not identified differences in risks of OAG by ethnic group within black populations [5, 25]. Under-powered sample sizes may be a reason why they could not detect ethnic differences in those studies. The Nigeria Blindness Survey had relatively large numbers of the main ethnic groups, giving adequate power to detect significant associations and differences within the black population. One of the potential reasons for the ethnic differences we observed may be the differential susceptibility due to larger optic discs. As reported in the normative data for the classification of glaucoma in prevalence surveys in Nigeria, the 97.5th percentile VCDR for the Igbo was 0.7 compared to 0.6 for the Fulani. Interestingly, the 99.5th percentile for IOP was

Table 1 Distribution of participants with and without open-angle glaucoma by socio-demographic, biophysical and ocular characteristics

	Without OAG [control]		OAG [cases]	
Total participants $N = 12{,}946$	$n = 12{,}738$ (96.5 %)		$n = 462$ (3.5 %)	
	n	%	*n*	%
Socio-demographic factors				
Age group (years)				
40 – 49	4760	37.4	45	9.7
50 – 59	3415	26.8	75	16.2
60 – 69	2550	20.0	124	26.9
70 – 79	1439	11.3	141	30.5
80+	574	4.5	77	16.7
Age (years) Mean ± SD	55.4 ± 12.1		66.2 ± 12.3	$p < 0.001$
Gender				
Female	6940	54.5	221	47.8
Male	5798	45.5	241	52.2
Ethnic group[a]				
Hausa	3191	25.2	78	16.9
Yoruba	2478	19.5	95	20.6
Igbo	1752	13.8	114	24.7
Fulani	801	6.3	20	4.3
Kanuri	326	2.6	13	2.8
Tiv	328	2.6	10	2.2
Ijaw	234	1.8	11	2.4
Urhobo	231	1.8	5	1.1
Ibibio	199	1.6	7	1.5
Nupe	198	1.6	8	1.8
Others	2946	23.2	100	21.7
Literacy				
Literate	5618	44.1	159	34.4
Illiterate	7120	55.9	303	65.6
Place of residence				
Rural	9883	77.6	354	76.6
Urban	2855	22.4	108	23.4
Biophysical factors				
Blood pressure (mmHg)[a]				
Normal	9343	73.8	308	67.2
Hypertension ≥140/90 mmHg	3315	26.2	150	32.8
Random blood glucose (mmol/L)[a]				
Normal	1551	97.1	98	96.1
Diabetes ≥11.1 mmol/L	47	2.9	4	3.9
Body mass index[a]				
Normal 18.5–24.9 kg/m^2	7672	61.1	276	60.6
Underweight <18.5 kg/m^2	1365	10.9	74	16.3
Overweight 25.0–29.9 kg/m^2	2464	19.6	75	16.5
Obese ≥30.0 kg/m^2	1060	8.4	30	6.6

Table 1 Distribution of participants with and without open-angle glaucoma by socio-demographic, biophysical and ocular characteristics *(Continued)*

Ocular factors[b]			
Total eyes *N* = 26,316 (100 %)	25,634 (97.4 %)	682 (2.6 %)	
Axial length (mm) Mean ± SD	22.63 ± 0.97	22.76 ± 1.09	*p = 0.001*
IOP (mmHg) Mean ± SD	14 ± 4	22 ± 11	*p < 0.001*

IOP intraocular pressure, *OAG* open-angle glaucoma, *SD* standard deviation
[a]missing values excluded; [b]ocular factors distribution by eyes

lower for the Igbo (22 mmHg) than for the Hausa (28 mmHg) [23] and this may imply that the Igbos have thinner corneas. However, a major limitation in interpreting this difference is the absence of pachymetry to measure central corneal thickness in the Nigeria Blindness Survey, which would have enabled corrected IOP estimates for comparison. Optic disc parameters are important in OAG with respect to attenuation of structural support, axonal protection and metabolic support provided by astrocytes [26]. These quantitative parameters are heritable traits [27, 28], thus genetic variation is another plausible reason for the ethnic differential risk. Genome-wide association studies (GWAS) in the African Caribbean population of Barbados, which has a high prevalence of OAG (6.8 %, 95 % CI 6.1–7.7 % in Blacks ≥40 years old) [15], confirmed two mechanisms of gene interaction with OAG: the absence of protective genes, and the presence of predisposing alleles increased the risk for OAG [29, 30]. Although the demographics of Barbados have been dynamic, and there are other socio-demographic and lifestyle factors that influence disease incidence [31] and progression [12, 32], the historical link between the Igbos and Barbadians lends credence to the genetic basis for the ethnic differences in risk of OAG seen in Nigeria.

Another interesting observation in our study was the strong association between low BMI (underweight) and OAG, albeit only in univariate analysis: presumably because of age, as older persons have lower BMI especially when of poor socioeconomic status. Higher BMI has been reported to be protective for OAG in Barbados [12] and Rotterdam [33]. Systemic inflammatory process [34] are possible linking factors which may also result in weight loss from general debilitation.

Our study did not find significant difference in risk for OAG in urban compared to rural population as seen in urban South India where the prevalence of OAG was more than doubled than in the rural population [16]; and possible associations with hypertension or diabetes were not statistically significant.

All studies have shown increasing age to be a risk factor for OAG [12, 31, 32, 35–43]. Indeed, in the Barbados Eye Study a 4 % increase in the relative risk of OAG per year was reported [31], and comparable to 6 % higher odds of OAG per year in this study. Increasing mitochondrial dysfunction in retinal ganglion cells and increased vulnerability of the optic nerve to neurodegeneration from oxidative stress serve as possible links between ageing and increased risk for OAG [44, 45].

This study also demonstrated that higher IOP has an independent association with OAG, as in numerous other studies. Higher IOP was an independent risk factor for glaucoma despite a large number of eyes having IOPs lower than the ‘upper limit of normal’ i.e. mean (+2SD) [40]. In the National Blindness Survey, 56 % of glaucoma eyes had IOP <22 mmHg; the mean IOP in glaucoma eyes was 23 (SD12) mmHg and the mean IOP in non-glaucoma eyes was 14 (SD4) mmHg [9]. This underscores the role of IOP as a tool for monitoring response to treatment rather than as a diagnostic factor.

Men had higher odds of OAG but only in univariate analysis. An increased risk of OAG in men has been reported in previous prevalence studies in Barbados, United States [12, 32] and Singapore [43], and in a Bayesian meta-analysis, men were more likely to have POAG than women (OR 1.36, 95 % CI 1.23–1.52) [1]. Further incidence studies are needed to clarify gender differences in risks of OAG.

Some studies have addressed associations between ocular perfusion factors (IOP, BP and MOPP) and OAG which suggest that vascular insufficiency is an important factor in OAG [31, 38, 46], as was in our study, higher BP and lower MOPP were significantly associated with higher odds of OAG.

Longer ocular axial length has been associated with OAG [37, 47]. In the Nigeria Blindness Survey axial length was longer in OAG eyes and was significantly associated with OAG, but this was not an independent risk factor after adjusting for age, IOP and other variables. In our study we assessed axial length rather than myopia as a potential risk factor because there was a high prevalence of nuclear lens opacities (8.8 %, 95 % CI 7.5–10.1) [48] which would increase

Table 2 Open-angle glaucoma and association with potential risk factors

	All eyes	OAG	Univariate analysis			Multivariate analysis		
	n (%)	*n* (%)	OR	95 % CI	*p*-value	OR	95 % CI	*p*-value
	26,316 (100 %)	682 (2.6 %)						
Socio-demographic factors								
Age (years)	(Min 40)		Reference			Reference		
Increasing age	(Max 100)		1.06	1.06–1.07	<0.001	1.04	1.03–1.05	<0.001
Gender	Female	328 (2.3)	Reference			Reference		
	Male	354 (2.9)	1.29	1.06–1.57	0.01	1.23	0.94–1.61	0.13
Ethnic group	Hausa	113 (1.7)	Reference			Reference		
	Yoruba	150 (2.9)	1.71	1.24–2.36	0.001	1.10	0.75–1.63	0.62
	Igbo	167 (4.5)	2.70	1.98–3.68	<0.001	1.73	1.18–2.56	0.01
	Fulani	31 (1.9)	1.09	0.65–1.85	0.73	1.18	0.65–2.19	0.58
	Kanuri	20 (2.9)	1.72	0.92–3.23	0.09	1.81	0.90–3.63	0.10
	Tiv	15 (2.2)	1.30	0.64–2.62	0.47	1.03	0.42–2.52	0.96
	Ijaw	14 (2.9)	1.69	0.86–3.35	0.13	1.51	0.50–4.60	0.47
	Urhobo	7 (1.5)	0.85	0.32–2.23	0.74	0.69	0.24–1.97	0.48
	Ibibio	10 (2.4)	1.43	0.62–3.27	0.40	1.29	0.58–2.89	0.53
	Nupe	9 (2.2)	1.29	0.59–2.79	0.52	1.25	0.58–2.67	0.57
	Others	144 (2.4)	1.38	1.01–1.90	0.05	1.13	0.75–1.70	0.57
Literacy	Literate	235 (2.0)	Reference			Reference		
	Illiterate	447 (3.0)	1.50	1.22–1.84	<0.001	1.06	0.79–1.42	0.70
Place of residence	Rural	527 (2.6)	Reference			Reference		
	Urban	155 (2.6)	1.02	0.81–1.28	0.88	1.14	0.85–1.54	0.38
Biophysical factors								
Hypertension	Normal	454 (2.4)	Reference			NI		
	Hypertension	223 (3.2)	1.38	1.12–1.70	0.002			
Blood pressure (severity of hypertension)	Normal	454 (2.4)	Reference			Reference		
	stage 1 mild	110 (2.7)	1.15	0.88–1.51	0.31	0.87	0.57–1.33	0.52
	stage 2 moderate	68 (3.7)	1.61	1.16–2.24	0.01	1.05	0.58–1.90	0.87
	stage 3 severe	45 (4.4)	1.91	1.27–2.88	0.002	1.05	0.45–2.45	0.90
Systolic BP	(Min 60)		Reference			NI		
	(Max 259)		1.01	1.01–1.02	<0.001			
Diastolic BP	(Min 35)		Reference			NI		
	(Max 157)		1.01	1.00–1.02	0.002			
RBG[a]	Normal	141 (4.3)	Reference			NI		
	Diabetes	4 (4.1)	0.94	0.33–2.67	0.91			
Body mass index (Categories)	Normal	406 (2.6)	Reference			Reference		
	Underweight	116 (4.0)	1.60	1.21–2.10	0.001	1.29	0.91–1.83	0.16
	Overweight	111 (2.2)	0.85	0.65–1.12	0.26	0.82	0.58–1.17	0.27
	Obese	42 (1.9)	0.75	0.50–1.12	0.16	1.18	0.71–1.96	0.52
Ocular factors								
Axial length (mm)	(Min 18.4)		Reference			Reference		
	(Max 30.0)		1.14	1.03–1.26	0.01	0.99	0.89–1.10	0.88
IOP (mmHg)	(Min 5)		Reference			Reference		
	(Max 50)		1.21	1.18–1.23	<0.001	1.22	1.18–1.25	<0.001

Table 2 Open-angle glaucoma and association with potential risk factors *(Continued)*

MOPP (mmHg)	(Min 6)	Reference			Reference		
	(Max 115)	0.96	0.95–0.97	<0.001	1.01	0.99–1.03	0.40

BP blood pressure, *IOP* intraocular pressure, *MOPP* mean ocular perfusion pressure, *NI* not included in multivariable models, *OAG* open-angle glaucoma, *RBG* random blood glucose

[a]tested for 1641 persons only

the risk of index myopia; and a relatively low prevalence of myopia ≤0.5D (after excluding persons with lens opacity, 9.4 %, 95 % CI 8.7–10.2) [49].

A strength of the Nigeria Blindness Survey is that it was nationally representative and had a large sample size with adequate power to detect statistical associations. A range of ethnic groups was represented in large enough numbers to allow comparison of risk between the largest ethnic groups in Nigeria. As part of the study protocol, not all participants had gonioscopy done and we did not record the presence of pseudoexfoliation (PXE). Hence, PXE was not assessed as a risk factor for OAG. In addition, some eligible participants did not have gonioscopy performed due to damage to the mirrors on the gonioscopy lenses by high humidity; and did not have Van Herick's AC angle estimation due to structural ocular pathology. Another limitation was that IOP was measured once and it was not interpreted using central corneal thickness, which was not measured. Additionally, visual field analysis was by FDT and participants classified as glaucoma did not undergo Humphrey visual field analysis (HFA). We were also not able to obtain information on duration of hypertension, history of cardiovascular disease or use of antihypertensive medication. However, this may not have a significant impact as only 14 % of participants reported being hypertensive [18]. Additionally, we did not obtain information on family history of glaucoma which would not have been reliable in this context. Indeed, only 5.6 % of those identified with OAG knew they had the condition [9].

This is the first time that an association of OAG has been observed with some ethnic groups. It is imperative that this finding be replicated in further studies as it may be a chance finding. While cultural or other practices might underlie the differences, or failure to fully adjust for confounders, given the relative lack of environmental factors identified to date for OAG, these observations suggest the need for a molecular genetics study of glaucoma in Nigeria. This might be included within a follow-up study on the cohort of the Nigeria Blindness Survey to explore the natural history and incidence of glaucoma, and the influence of immunological markers of inflammation.

Conclusion

This study gives us risk factors data on OAG and confirms that OAG is a public health problem in people ≥40 years. As a public health strategy, opportunistic eye examination, case detection and examination for OAG need to be performed on all people aged ≥40 years and the ethnic groups most at risk.

Abbreviations

AC, Anterior chamber; BMI, Body mass index; BP, Blood pressure; CI, Confidence intervals; DBP, Diastolic blood pressure; FDT, Frequency doubling technology; GWAS, Genome-wide association studies; IOP, Intraocular pressure; ISGEO, International Society of Geographical and Epidemiological Ophthalmology; MOPP, Mean ocular perfusion pressure; OAG, Open-angle glaucoma; OR, Odds ratio; RAPD, Relative afferent pupillary defect; RBG, Random blood sugar; SBP, Systolic blood pressure; SD, Standard deviation; VA, Visual acuity; VCDR, Vertical cup:disc ratio; WHO, World Health Organization.

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Availability of data and materials

Data are currently with the authors as the study is on-going. It will be deposited with the Director, Health Planning, Research and Statistics, Federal Ministry of Health, Abuja, Nigeria.

Authors' contributions

FK and CG developed the study concept and design. FK, MA, RW, JE, WN, GVSM and CG were involved in acquisition, analysis, or interpretation of data. The manuscript was drafted by FK and edited by RW and CG. FK, AM, RW, JE, WN, GVSM and CG critically revised the manuscript for important intellectual content. Statistical analysis was done by FK and JE. FK and CG obtained funding. The study was supervised by FK, RW, WN, GVSM and CG. All authors have read and approved of the final version of the manuscript.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical approval was obtained from the Ethics Committee of the London School of Hygiene & Tropical Medicine and the Federal Ministry of Health of Nigeria. Oral informed consent was obtained from community leaders, heads of households and all participants. The study adhered to the tenets of the declaration of Helsinki. Participants with treatable ocular conditions were referred and cataract blind participants were offered surgery.

Previous presentation

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Chapter 9

Ethnicity and deprivation are associated with blindness among adults with primary glaucoma in Nigeria

Results from the Nigeria National Blindness and Visual Impairment Survey

Participants arriving for a focus group discussion in the community

Research paper determining the risk factors associated with glaucoma blindness

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RESEARCH PAPER COVER SHEET

PLEASE NOTE THAT A COVER SHEET MUST BE COMPLETED FOR EACH RESEARCH PAPER INCLUDED IN A THESIS.

SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Journal of Glaucoma		
When was the work published?	July 2016; Epub ahead of print		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	No. Work included is in accepted manuscript format	Was the work subject to academic peer review?	Yes

**If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.*

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I collected data as part of the survey team. I developed the glaucoma diagnostic algorithm. I performed the statistical analyses. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors.

Student Signature: Kyari **Date:** 28 August 2016

Supervisor Signature: CGilbert **Date:** 30 August 2016

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Title:

Ethnicity and deprivation are associated with blindness among adults with primary glaucoma in Nigeria.

Results from the Nigeria National Blindness and Visual Impairment Survey.

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Abstract

Purpose: We explored the risk factors for glaucoma blindness among adults aged ≥40 years with primary glaucoma in Nigeria.

Participants and methods: 13,591 participants aged ≥40 years were examined in the Nigeria National Blindness and Visual Impairment Survey; 682 (5.02%, 95CI 4.60-5.47%) had glaucoma by ISGEO's criteria. This was a case-control study (n=890 eyes of 629 persons): glaucoma blind were cases and glaucoma not-blind were controls. Education level and occupation were used to determine socioeconomic status scores, which were divided into three tertiles (affluent, medium and deprived). We assessed socio-demographic, biophysical and ocular factors by logistic regression analysis for association with glaucoma blindness. Multinomial regression analysis was also performed with non-glaucoma as the reference category.

Results: 119/629 (18.9%; 95%CI 15.9-22.4%) persons were blind in both eyes, leaving 510 as controls. There was inter-ethnic variation in odds of blindness; age, male sex, socio-economic status, prior diagnosis of glaucoma, hypertension, intra-ocular pressure and lens opacity were associated with glaucoma blindness. Axial length, mean ocular perfusion pressure and angle-closure glaucoma were associated with blind glaucoma eyes. In multivariate analysis, Igbo ethnicity (OR2.79, 95%CI 1.03-7.57) had higher risk as was being male (OR4.56, 95%CI 1.72-12.09), and unmarried (OR2.46, 95%CI 1.03-5.93). Deprivation (OR3.72, 95%CI 1.55-8.93), prior glaucoma diagnosis (OR5.45, 95%CI 1.67-17.74) and higher intraocular pressure (OR1.07, 95%CI 1.02-1.13) were also independent risk factors for glaucoma blindness.

Conclusion: Approximately 1 in 5 people with primary glaucoma were blind. Male sex, ethnicity and deprivation were strongly associated with blindness. Services for glaucoma need to improve in Nigeria, focusing on poor communities and men.

Key words: glaucoma blindness; ethnicity; deprivation; risk factors; population-based; Nigeria.

Running head – Blindness among adults with glaucoma in Nigeria

Introduction

Glaucoma is the leading cause of irreversible blindness worldwide.[1] Although there are very few population-based blindness prevalence surveys in Africa,[2] data suggest that the prevalence of glaucoma blindness in Africa is the highest in the world.[3, 4] In sub-Saharan Africa, the proportion of people with glaucoma identified in population-based surveys who are blind is alarming. In Ghana (2001) 10% of participants aged 30 years and above with glaucoma were blind.[5] Among participants aged 40 years and above, the proportion of people with glaucoma who were blind was 14% in Kongwa, Tanzania (1996),[6] 15% in Mamre, South Africa (1992),[7] and 33% in Temba, South Africa (1998).[8] Glaucoma occurs all over the world,[9] but risks for glaucoma blindness vary.[10, 11] Early diagnosis and treatment delay vision loss and prevent blindness from glaucoma[12] as the rate of progression of optic nerve damage is slowed by treatment.[13, 14] Recent advances in technology for diagnosing glaucoma, greater therapeutic options, and treatment monitoring have decreased the probability of glaucoma blindness in patients in the care system in industrialized countries.[15] Conversely, without treatment there is a very high rate of progression of visual field loss.[16] Who goes blind from glaucoma is influenced by biomedical factors such as age at onset, duration of disease and rate of progression of glaucoma.[17, 18] In many low income settings aggravating factors relating to the health care system include low provision of glaucoma services and access to services,[17-20] poor quality of care,[21] and inadequate compliance with treatment and follow-up,[18, 20] the latter being compounded by low levels of education.[22] Few studies of risk factors for glaucoma blindness have been undertaken in Africa where glaucoma has an earlier age of onset and a more aggressive course. Services for glaucoma are also inadequate and acceptance and compliance with treatment are low.

The increase in susceptibility of retinal ganglion cells to premature death may be mediated by genetic factors which may also interact with environmental factors.[23] Family studies and genome-wide association studies (GWAS) for open-angle glaucoma (OAG) have demonstrated genotype-phenotype correlations of heritable ocular features such as central corneal thickness (CCT),[24] optic disc size, vertical cup:disc ratio (VCDR)[25] and intraocular pressure (IOP).[26] However, only one molecular genetics study of glaucoma has been undertaken to date in Africa and the investigators did not observe significant association with any of the previously reported genes and loci in OAG cases in the Ghana study population.[27] Determining variation in the susceptibility to and severity of glaucoma among different ethnic groups who share common ancestry, is a first step in assessing the role of genetic factors in the pathogenesis of OAG in Africa. In an earlier study arising from the Nigeria National Blindness and Visual Impairment Survey (hereafter referred to as the Nigeria Blindness Survey) 94% of glaucoma was undiagnosed and untreated, and the crude prevalence was significantly higher in the Igbo ethnic group (7.77%; 95%CI 6.57-9.16).[28] In this paper we present findings on risk factors for blindness, including ethnic groups, among those identified with glaucoma during the Nigeria Blindness Survey.

The Nigeria Blindness Survey was the largest population-based blindness survey ever undertaken in Africa, providing data on the major blinding diseases,[29] including glaucoma which was the second commonest cause (16.7%).[30] The prevalence of blindness in adults aged ≥40 years was 4.2% (95%CI 3.8-4.6)[31] and the glaucoma-specific blindness prevalence was 0.7% (95%CI 0.6-0.9).[30] Systematic sample of 1-in-7 participants provided normative values[32] for defining glaucoma using the International Society of Geographic and Epidemiology Ophthalmology (ISGEO) levels of evidence.[33] The prevalence of glaucoma of all types was 5.02% (95%CI 4.60-5.47), one-fifth of whom were blind in both eyes.[28]

Materials and Methods

Details of the methods used in the Nigeria Blindness Survey,[29] normative values for diagnosing glaucoma[32] and the prevalence and types of glaucoma in Nigeria[28] have been published; and data on risk factors for OAG have been accepted for publication. A summary of the clinical assessments, with particular reference to classification of glaucoma and how potential risk factors for glaucoma blindness were measured and categorised, are described here.

Ethics

Ethical approval was obtained from the Ethics Committee of the London School of Hygiene & Tropical Medicine and the Federal Ministry of Health, Nigeria. Informed consent was obtained from community leaders, heads of households and all participants. The study adhered to the tenets of the declaration of Helsinki. Persons with medical or eye conditions including glaucoma needing further assessment and treatment were referred to the nearest healthcare facility.

Study design and study population

The study design for the analysis of risk factors for glaucoma blindness was a case-control study: people with glaucoma that were blind in both eyes (visual acuity [VA] worse than 3/60 in the better eye) were classified as cases; and people with glaucoma but not blind were classified as controls. For analysis of risk of blindness in eyes with glaucoma, the cases were glaucoma eyes that were blind (VA worse than 3/60) and the controls were glaucoma eyes that were not blind. The analysed sample consisted of persons classified as glaucoma and with no identified features suggesting secondary glaucoma (Figure 1). A person was classified as having glaucoma if the condition was present in one or both eyes. The sample size calculated for the Nigeria Blindness Survey was 15,375 persons aged $\geq$40 years in 310 clusters.[29]

Data collection and clinical assessment

Participants were invited to a temporary examination site set up within the community. All were interviewed to obtain relevant personal and socio-demographic data. Evidence of glaucoma surgery, presence of cataract and evidence of cataract surgery were noted. Some investigations were not possible in participants who could not come to the examination center and who were examined in their home.

Glaucoma classification

Glaucoma was classified according to the ISGEO criteria, using percentile distributions of VCDR, VCDR asymmetry and IOP in *normal* Nigerians, derived from the normative subset (n=1759) of this study population.[32] The diagnosis of glaucoma started with VCDR findings. Level 1 classification required structural and functional evidence i.e. 97.5th percentile of the VCDR (≥0.7) or VCDR asymmetry (≥0.1) in our normal population and visual field loss typical of glaucoma. Level 2 required advanced structural damage i.e. 99.5th percentile VCDR (≥0.75) or VCDR asymmetry (≥0.2) in the absence of visual field evidence. Level 3 applied when the optic disc was not seen and visual field testing was not possible, and used: a) blindness (VA<20/400) with the 99.5th percentile IOP (≥28mmHg), or b) diagnosed with/being treated for glaucoma. An additional level of evidence (level 2b) was added where the optic disc was visualized but the VCDR was <99.5th percentile and there were no visual fields available, but there was other compelling evidence such as RAPD, high IOP and/or corneal edema. These cases were adjudicated by glaucoma specialists (RW and WN). A person was said to have glaucoma if there was glaucoma in one or both eyes.

Visual acuity measurement and definition of blindness

Presenting VA was assessed by a trained ophthalmic nurse using a reduced logMAR tumbling-E chart[34, 35] at 4 meters. If the participant could not see any letters at 4 meters, testing was repeated at 1 meter. Participants unable to see any letters at 1 meter were assessed for counting fingers, hand movement or perception of light (PL) or no PL (NPL). Visual acuities were categorized using World Health Organization (WHO) definitions of blindness and visual impairment (VI)[36] where blindness at the person level is defined as VA worse than 3/60 in the better eye. An eye was classified as blind if the VA was worse than 3/60 in the affected eye.

Determining the cause of blindness

All participants with a VA worse than 6/12 in one or both eyes were examined by the experienced ophthalmologist. All disorders that may have contributed to visual loss in each eye were determined from a list of disorders. The principal/main cause was then selected for each eye and then for the person in the order of most preventable cause first (e.g. corneal opacity) then most treatable (e.g. refractive errors, cataract) and then other avoidable causes (e.g. glaucoma). Causes of blindness were determined using the World Health Organization's algorithm for use in surveys, which emphasizes treatable and preventable causes. In the Nigeria survey, glaucoma was only assigned as the cause if, in the view of the examiner, other more readily treatable causes, such as clinically significant cataract were not present. For example, in a blind person with clinically significant cataract and glaucoma, the main cause of blindness would be cataract.

In this paper, *glaucoma blindness* refers to a person with glaucoma in one or both eyes and with a VA of worse than 3/60 in the better eye. A *blind glaucoma eye* has glaucoma with VA worse than 3/60 in the affected eye.

Risk factors assessment and classification

Variables were analysed as continuous (age, axial length, IOP and mean ocular perfusion pressure [MOPP]) or binary (sex, marital status, literacy, place of residence, history of glaucoma, presence of hypertension, random blood glucose level [RBG], lens opacity, type of glaucoma and history of glaucoma surgery); or categorised into groups (ethnicity, socio-economic status [SES], geo-political zone [GPZ], severity of hypertension and body mass index [BMI]).

Participants were asked about their ethnicity, marital status, ability to read and/or write, education level and occupation. Ethnic groups represented by $\geq$200 participants were analysed separately (Fulani, Hausa, Ibibio, Ibo, Ijaw, Kanuri, Nupe, Tiv, Urhobo and Yoruba). Marital status was classified as married and unmarried (single, divorced or widowed). Being literate was any ability to read and/or write, otherwise the participant was classified as illiterate. Proxies were used to determine household SES. Occupations were ranked from zero (not employed) to seven (professional) and the highest level of school attended were from zero (no schooling) to four (tertiary education). The sum of these scores were calculated for each individual and the mean of sum of these ranks within the household was assigned as the SES score for each individual in order to take into account of heterogeneity and household size. The SES scores were further divided into 3 equal tertiles as deprived, medium and affluent. Rural place of residence was defined as a settlement with a population of ≤20,000 residents, and GPZ are the 6 administrative zones in Nigeria – North Central, North East, North West, South East, South South and South West.

Blood pressure (BP) was measured with the Omron wrist instrument (Omron Healthcare Ltd, Milton Keynes, England). The average of three readings was used in analysis. Hypertension was defined as BP≥140/90mmHg and severity was categorised using WHO categories: stage 1 for systolic/diastolic BP≥140/90 mmHg, stage 2 ≥160/100 mmHg and stage 3 ≥180/110 mmHg.[37] BMI was calculated by dividing body weight (kg) by height (m) squared and categorised according to the international classification i.e. underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (25.0–29.9kg/m^2) and obese (≥30.0 kg/m^2).[38] Every 1-in-7 participants and all participants suspected to have diabetic retinopathy on examination had RBG tested with One-touch ultra blood glucose meter (LifeScan, UK), and grouped as normal (<11.1 mmol/L) or raised (≥11.1mmol/L).[39]

Ocular axial length was measured by ultrasound A-scan biometry (Bioline Biometer OPTIKON 2000 S.p.A Roma, Italy) and IOP was measured by Goldmann applanation tonometry using standard methods. To explore the association of vascular perfusion and glaucoma blindness, MOPP was calculated from diastolic BP (DBP), systolic BP (SBP) and IOP as $^{2}/_{3}$[DBP+$^{1}/_{3}$ (SBP-DBP)-IOP].[40] Lens grading was performed using the Mehra-Minassian[41] and the WHO grading systems.[42] Lens opacity was classified as positive if it was visually disabling and VA<6/12 in the affected eye.

The type of glaucoma was determined by gonioscopy without corneal compression performed with Volk's 1-mirror non-flanged lens and Van Herick's (VH) method for the estimation of the anterior chamber (AC) angle.[43] Grades 3 and 4 VH AC angle estimation had a 99.1% sensitivity and 93% positive predictive value in identifying open angles by gonioscopy (risk factors for OAG, paper submitted for publication). Thus glaucoma eyes in which Schwalbe's line could be seen, or had grades 3 or 4 by VH estimation if gonioscopy was not done, were classified as OAG. Glaucoma eyes in which Schwalbe's line could not be seen, or had grades 0, 1 or 2 by VH estimation if gonioscopy was not done, were classified as angle-closure glaucoma (ACG). The eyes were unclassified if there was no gonioscopy or VH estimation of the AC angle. Participants were asked about history of ocular surgery and examined for evidence of glaucoma surgery such as bleb and peripheral iridectomy.

Statistical analysis

Socio-demographic, biophysical and ocular factors were analyzed for associations with glaucoma blindness after identifying participants with primary glaucoma who were blind or not blind (Figure 1). Statistical analysis was performed using Stata/IC 13.0 (Stata Corp, College Station, TX).

We examined the association between glaucoma blindness and each risk factor separately and report odds ratios (OR) with 95% confidence intervals. We also assessed associations between blind glaucoma eyes and each of the six ocular factors. We used logistic regression to assess the independent effect of each risk factor on glaucoma blindness and blind glaucoma eyes and report adjusted odds ratios and 95% confidence intervals. Likelihood ratio tests and joint Wald tests were performed to check the fit of the model and the effect of levels of categorical variables and those with missing data. We assessed the variance inflation factor (VIF) for the covariates. Collinear variables were not included in the same

multiple logistic regression model. The following covariates were included and adjusted for in the main multivariable model for glaucoma blindness: age, sex, ethnicity, marital status, literacy, SES, rural/urban residence, history of glaucoma, BP, BMI, axial length, IOP, lens opacity and history of glaucoma surgery. The association of MOPP was explored in a model without BP and IOP. Associations for GPZ and type of glaucoma were explored in separate models. All eyes were analyzed to take into account bilateral cases and ocular variables for within-person correlation clustered for pairs of eyes, with robust standard errors.
To determine associations for a glaucoma eye being blind, all ocular variables were included in the multivariate model.

To explore the magnitude and direction of the relative risk ratios (RRR) of the two glaucoma outcomes (not-blind and blind) compared to the non-glaucoma group, we performed multinomial logistic regression analysis with the non-glaucoma subset as the reference category. The variables age-group, sex, ethnic group, marital status, literacy, SES and place of residence were included in the model. We tested the overall effect of each of the covariates and levels of ethnic group and SES on predicting the two glaucoma outcomes. The marginal predicted probability plot of glaucoma blindness by age-group with sex and with SES were produced. P-values <0.05 were considered as statistically significant. Missing values were excluded.

Results

In the study sample, 12,909 participants did not have glaucoma: 11,651 (90.3%) had both optic discs assessed and classified as non-glaucoma (Figure 1). For eyes that VCDR could not be assessed (n=1751 eyes, 6.8%), there was no level 3 evidence for glaucoma. In this analysis of risk factors for glaucoma blindness 890 eyes of 629 participants were included (Figure 1): 119 had glaucoma (18.9%; 95%CI, 15.9-22.4) and blind in both eyes (cases); and 510 controls. A further 139 participants with glaucoma had monocular blindness. Nearly half of those with glaucoma (258; 41%) were therefore blind in at least one eye. Glaucoma was the main cause of blindness in both eyes of 60/119 persons (50.4%) and in one eye of 31 persons. Thus glaucoma was the main cause of blindness in at least one eye of 91/119 (76.5%). Other main causes of blindness were cataract, optic atrophy and macular degeneration. The main cause of blindness at the person level in the 119 participants was glaucoma in 83 (70%) and cataract in 16 (13%)(Table 1). Of the 890 eyes with glaucoma included in the analysis there were a total of 323 (36.3%) blind eyes with glaucoma in 358 participants.

Glaucoma blind persons were older (mean age 68.5 years/SD 13.3) than the non-blind (mean age 63.4years/SD 13.0; p=0.0001)(Table 2). The number blind increased with increasing age up to the age-group 70-79 years.

There was a higher proportion of unmarried glaucoma blind participants than married. Stratified by sex, among the 43 unmarried glaucoma blind, 33 (76.7%) were women (p<0.001).

A history of prior glaucoma diagnosis was positive in 38/629 (6.0%) participants; 15.1% known to have glaucoma were blind compared with 3.9% of undiagnosed cases (Table 2).

The likelihood ratio tests on categorical covariates: ethnic group across all levels (p=0.001), BP groups (p=0.005) and SES (p<0.001) indicate that these variables create a statistically significant improvement in the fit of the main multivariable model; whereas for BMI categories (p=0.53) and type of glaucoma (p=0.27). For the joint Wald test (ethnic, BP, BMI) p-value is 0.001.

Risk factors associated with glaucoma blindness

Ethnicity and GPZ were not predictors of SES. In univariate analysis, people with glaucoma blindness were more likely to be older, male and in deprived households. They were also more likely to be known glaucoma and have hypertension, and the odds of blindness increased with increasing severity of hypertension (Table 4). The Igbo, Hausa, Fulani and Ijaw ethnic groups had significantly higher odds of glaucoma blindness than the reference ethnic group (Yoruba) (Table 3). Higher IOP (OR = 1.06; 95%CI 1.04-1.08; p<0.001) and presence of visually disabling lens opacity (vdLO) (OR = 2.72; 95%CI 1.89-3.91; p<0.001) also increased the odds of glaucoma blindness (Table 5).

In multivariate analysis, being male, living in a deprived household (see Table 3), severe hypertension (see Table 4) and higher IOP (see Table 5) remained independent risk factors for glaucoma blindness. Being poor/deprived had three-and-half times higher odds of glaucoma blindness (OR = 3.57; 95%CI 1.46-8.72; p=0.005) than affluent participants (Table 3). A prior diagnosis of glaucoma had a significantly higher odds of glaucoma blindness (OR = 5.89; 95%CI 1.79-19.40; p=0.004) (Table 3). Being unmarried was also an independent risk factor with higher odds of being blind (OR = 2.50; 95%CI 1.03-6.07; p=0.04). The Igbo and Fulani ethnic groups had higher odds for glaucoma blindness (Table 3).

Risk factors associated with blind glaucoma eyes

About half of the eyes with glaucoma and vdLO were blind (206/415; 49.6%), and almost two-thirds of eyes with ACG were blind (42/66; 63.6%)(Table 6). There was evidence of glaucoma surgery in 19/629 (3.02%) participants of whom eight had surgery in both eyes (total 27/890 eyes); all of which were trabeculectomy. There was no significant difference in blindness status in eyes that had undergone trabeculectomy.

In univariate analysis, longer axial length, higher IOP, lower MOPP, vdLO and ACG were significantly associated with blind glaucoma eyes. However, when adjusted for age, sex, ethnicity, marital status, SES, location and other factors in the multivariable model, only higher IOP (OR = 1.09; 95%CI 1.05-1.13) and vdLO (OR = 2.13; 95%CI 1.36-3.33) remained independent risk factors. There was no statistically significant association between trabeculectomy and glaucoma blindness or blind glaucoma eyes.

Relative risk of the two glaucoma outcomes (not-blind and blind) compared to non-glaucoma

RRR>1 signifies that there is an increase in the outcome (not-blind or blind) when compared to the reference group, non-glaucoma; given that the other variables in the model are held constant. Table 7 shows the frequency distribution and the RRR of the covariates for the two outcomes of glaucoma. The factors that increased the outcome for glaucoma are shown.

Glaucoma not-blind relative to non-glaucoma

Increasing age was the only independent factor that had an increased relative risk for glaucoma not-blind compared to non-glaucoma; from RRR 1.84 (95%CI 1.37-2.48) in the 50-59 years age-group to 6.69 (95%CI 4.63-9.67) in the 80+ year-olds (Table 7).

Glaucoma blind relative to non-glaucoma

Older age-groups were more likely to have glaucoma blindness, with a RRR increasing from 3.51 (95%CI 1.77-6.99) in the 60-69 years age-group to 10.08 (95%CI 4.85-20.93) in the 80+ year-olds.

The Igbo ethnic group had a non-statistically significant increase in relative risk for glaucoma not-blind (RRR = 1.18; 95%CI 0.91-1.54; p=0.21) but were more likely to be glaucoma blind by a factor of 3.71 (95%CI 2.01-6.85; p<0.001). Males were more likely than females to be glaucoma blind compared to non-glaucoma with an expected increase by a factor of 3.00 (95%CI 1.87-4.83).

Deprivation did not increase the outcome of glaucoma not-blind (RRR = 0.94; 95%CI 0.73-1.21). However, for people with glaucoma, the deprived were more likely than the affluent to be blind with glaucoma by a factor of 4.42 (95%CI 2.50-7.80). The overall effect of SES was statistically significant. More specifically, we tested the effect of deprivation in predicting glaucoma not-blind and glaucoma blind and this showed that the effects were statistically different from each other, i.e. the deprived were not at higher risk than the affluent to have glaucoma but were more likely to be blind with it. The Igbo, Hausa and Fulani ethnic groups also showed different effects in outcome of glaucoma (Table 7).

Figure 2 shows the marginal predicted probabilities of glaucoma blindness by increasing age and by SES. For a 70-79 year-old male, the average marginal probability of being glaucoma blind was about 3.5% compared to 1% for a female of the same age group.

Compared to the affluent, deprivation increased the average marginal probability of glaucoma blindness by approximately 0.5% in the younger age group, to 4% in 70-79 year age-group and over 5% in the 80+ ages.

Discussion

To our knowledge, this is the first population-based study of risk factors for blindness among individuals with glaucoma in a black population in Sub-Saharan Africa. In this study the vast majority of participants with glaucoma had undiagnosed and untreated disease (96%) at the time of the survey, and so the findings largely reflect the natural history of untreated glaucoma.
A set of post-estimation statistical analysis tools that would aid the understanding, interpretation and presentation of the relationship between the assessed risk factors were used. Being of Igbo ethnicity was an independent risk factor for glaucoma blindness. The Fulani, Ijaw and Tiv ethnic groups had odds ratios with very wide confidence intervals hence we cannot draw meaningful conclusions on these. Those with higher IOP and vdLO, being male and those living in deprived households also had increased odds of blindness.

Although there are over 250 languages spoken in Nigeria, each ethnic group has similar ancestry and may be of common genetic stock. As ethnic group did not correlate with socio-economic status, ethnic differences in risk of glaucoma blindness suggest that there may be genetic similarities that lead to more aggressive disease in some ethnic groups, in terms of higher IOP or greater susceptibility of the optic nerve head to glaucoma, or gene-environment interactions. In the Nigeria Blindness Survey, about half (56%) of the eyes with glaucoma had IOP $\leq$22mmHg (mean IOP+2SD),[28] and there was variation in optic disc parameters as well as IOP among some ethnic groups.[32] These data are being explored to assess whether different ethnic groups are at increased risk of normal tension glaucoma, which may reflect genetic susceptibility to structural optic nerve damage (as in the Japanese population, for example),[44] or have differing frequencies of genetic variants such as CDKN2BAS associated with normal tension glaucoma.[45]

Most of earlier studies have been retrospective, facility-based studies of glaucoma patients in the care system, showing that severity of glaucoma at diagnosis and poor control of IOP were key risk factors for progression to blindness.[46-50] They buttress the paradigm that glaucoma visual loss could be prevented by earlier diagnosis and consistent and adequate treatment with IOP lowering as the cornerstone. Hospital reviews in Nigeria and sub-Saharan Africa also highlight factors that limit glaucoma patients' ability to access or maintain treatment, thus worsening their visual prognosis.[51-56] One population-based study reported older age as the only factor associated with progression/severity of glaucoma in untreated individuals who were re-examined after 10 years of the initial survey.[16] In our study a staggering 1-in-5 people with glaucoma were already blind suggesting that services for glaucoma are either not available or poorly accessible. This is in contrast to data from a glaucoma clinic in Scotland, where glaucoma blindness was uncommon.[57] In Norwich, Ang and Eke's review of treated glaucoma patients reported 3.3% blind, none of whom was certified due to glaucoma.[58] However, in Sweden glaucoma patients had a lifetime risk of glaucoma blindness of 15%.[59] These studies did not include those undiagnosed in the population and may have overestimated the risk of glaucoma blindness.

In our study, not all blindness was due to glaucoma and at least 13% could have been prevented by cataract surgery. Highlighting this and other causes underscores the need for providing non-glaucoma interventions. The low cataract surgical coverage in this population[60] compounds the problem. Hence there is a need for integrated comprehensive eye care services and high quality cataract surgery in patients with glaucoma.

A surprising finding was that men were at a considerably higher risk of glaucoma blindness. This is likely to reflect the significantly higher prevalence of glaucoma in men (5.67%; 95%CI 5.05-5.47) than women (4.47%; 95%CI 3.98-5.00; $p=0.002$)[28] and also an indication of general lack of availability or access to glaucoma services. Being unmarried was also an independent risk factor for glaucoma blindness, particularly among women. This finding probably reflects disempowerment of unmarried women whose health needs are not prioritized by other family members or the community. In our study, those living in deprived households were also at a considerably higher risk of glaucoma blindness and poor old people were most affected. As in most studies and reviews of poverty and blindness, socio-economic status tends to influence health-seeking behavior, awareness and healthcare access.[61-66] Rural/urban and GPZ location were not independent risk factors in this study, suggesting that services for glaucoma are equally poor across the country. As in the St Lucia study,[16] increasing age was associated with glaucoma blindness, but the association was not significant in multivariate analysis. This may signify that glaucoma occurs at an earlier age in Nigeria with blindness occurring across all age groups, as duration of disease is an important risk factor for blindness.[49, 67] Blindness occurring at an earlier age has also been reported in the black population of Baltimore.[68]

A prior diagnosis of glaucoma was independently associated with blindness. Many facility-based studies in Africa show that a high proportion of newly diagnosed glaucoma patients present with very advanced disease;[19, 51-54, 69] and diagnosed cases were more severely affected than non-diagnosed cases in the population.[13] This underscores the need for an integrated approach for earlier case-finding in the community, and the need for services that are acceptable and affordable.

There are some limitations in this study. The definition of blindness by VA alone would underestimate the total numbers blind from glaucoma. Including visual fields in the definition of blindness might have increased the estimates of blindness by up to 25%.[70] SES was determined by proxy factors i.e. education and occupation rather than using asset scores or other measures as this was not feasible within the constraints of the survey. Data on the duration of glaucoma or of blindness were not collected, as these data would be subjective and unreliable.

The combination of high prevalence of glaucoma, socioeconomic deprivation and lack of access to services means that in Nigeria glaucoma is often a blinding condition. The finding that some ethnic groups are at increased risk of glaucoma and of glaucoma blindness warrants further investigation from a molecular genetics perspective which may further our understanding of the pathogenesis of glaucoma in African populations and among those of African ancestry who live elsewhere.

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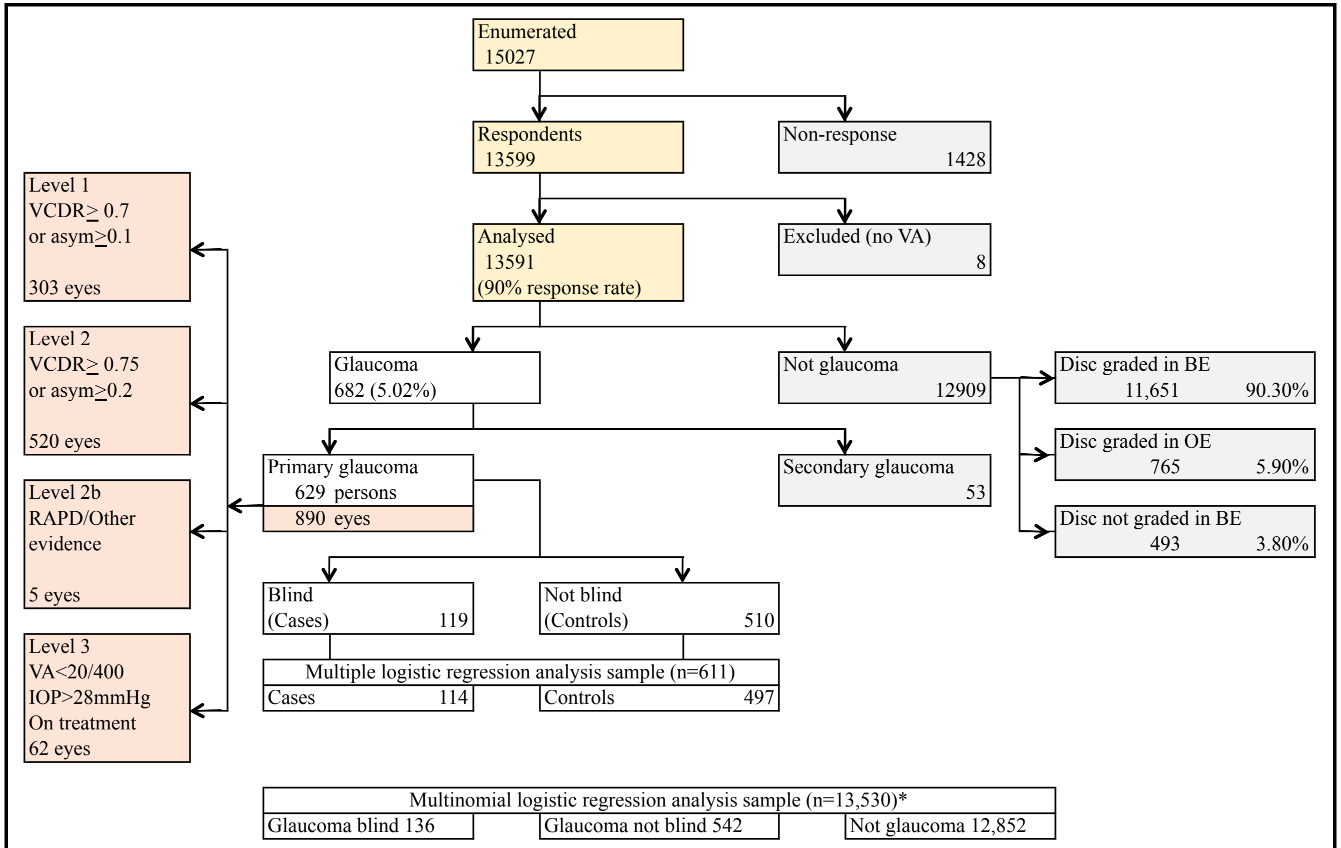
Figure 1. Selection of Cases and Controls for Analysis of Risk Factors for Glaucoma Blindness and Classification of Glaucoma Eyes by Levels of Evidence



VA = visual acuity; BE = both eyes; OE = one eye; VCDR = verical cup:disc ratio; asym = VCDR asymmetry; RAPD = relative afferent pupillary defect; IOP = intraocular pressure. * = multinomial regression logistic sample includes primary and secondary glaucoma, 61 persons have missing data

Blind = VA<20/400 in the better eye

Figure 2. Marginal Predicted Probabilities of Glaucoma Blindness by Age-Group With Sex and With Socioeconomic Status

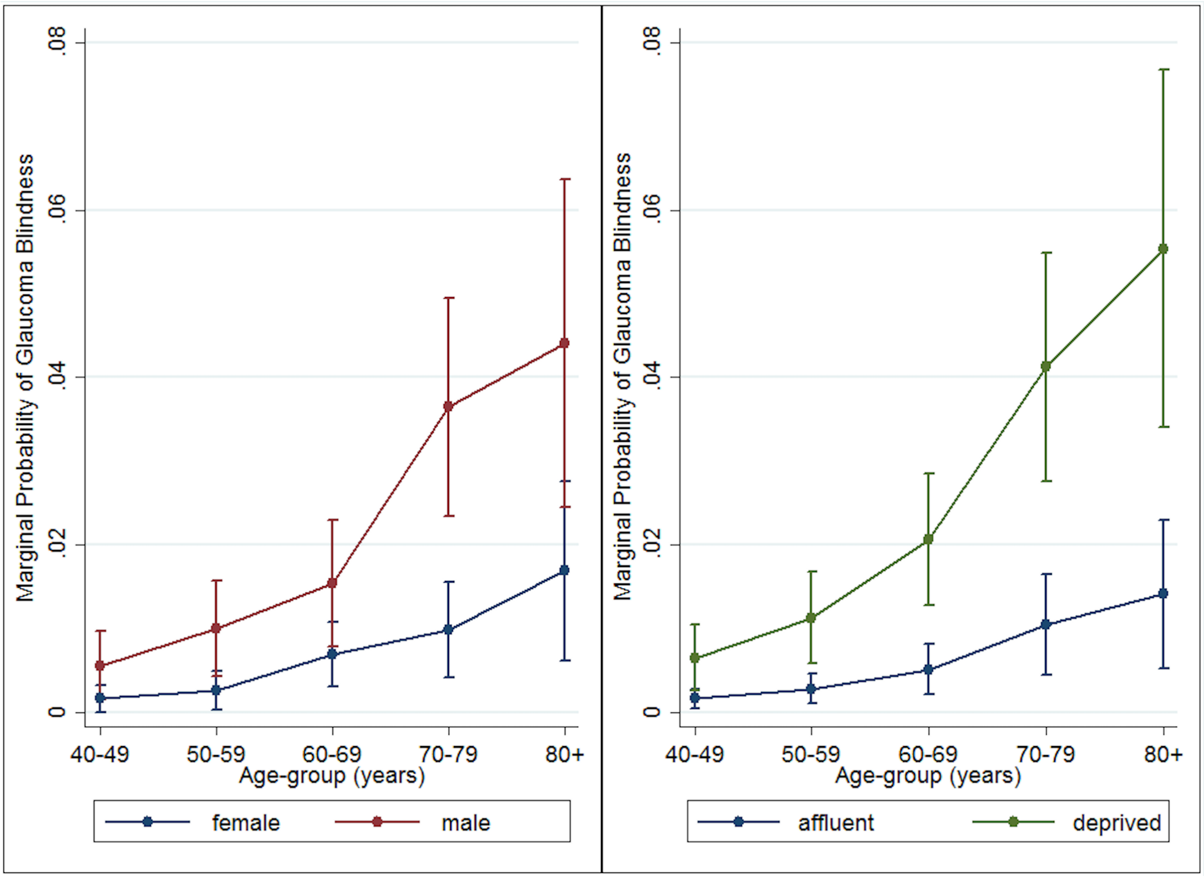


Table 1. Main Causes of Blindness in Participants With Primary Glaucoma

Main cause of blindness	**Number**	**%**
Glaucoma	83	69.8
Cataract	16	13.5
Optic atrophy	6	5.1
Macular degeneration	3	2.5
Other posterior segment disease	3	2.5
Corneal opacity	3	2.5
Uncorrected aphakia	2	1.7
Refractive error	1	0.8
Anterior uveitis	1	0.8
Unexplained	1	0.8
Total	119	100.0

Table 2. Distribution Of Glaucoma Participants With and Without Blindness By Socio-Demographic And Biophysical Factors (Total =629)

Variable		Not blind n (%)	Blind n (%)
		510 (81.1%)	**119 (18.9%)**
Socio-demographic factors			
Age group (years)	40 – 49	78 (15.3)	11 (9.2)
	50 – 59	105 (20.6)	14 (11.8)
	60 – 69	133 (26.1)	29 (24.4)
	70 – 79	125 (24.5)	37 (31.1)
	80+	69 (13.5)	28 (23.5)
	Mean±SD	63.4±13.0	68.5±13.3
Sex	Female	268 (52.5)	43 (36.1)
	Male	242 (47.5)	76 (63.9)
Ethnic group	Yoruba	132 (26.1)	15 (12.6)
	Igbo	112 (22.1)	30 (25.2)
	Hausa	86 (17.0)	24 (20.2)
	Fulani	16 (3.2)	10 (8.4)
	Kanuri	12 (2.4)	4 (3.3)
	Ijaw	10 (1.9)	5 (4.2)
	Ibibio	9 (1.8)	2 (1.7)
	Nupe	8 (1.6)	2 (1.7)
	Tiv	8 (1.6)	3 (2.5)
	Urhobo	7 (1.4)	0 (0.0)
	Others	106 (20.9)	24 (20.2)
Marital status	Married	355 (69.6)	76 (63.9)
	Unmarried	155 (30.4)	43 (36.1)
Literacy	Literate	182 (35.7)	41 (34.5)
	Non-literate	328 (64.3)	78 (65.5)
Socio-economic status	Affluent	138 (27.1)	17 (14.3)
	Medium	192 (37.6)	20 (16.8)
	Deprived	180 (35.3)	82 (68.9)
Place of residence	Urban	116 (22.7)	30 (25.2)
	Rural	394 (77.3)	89 (74.8)
Geo-political zone	South south	85 (16.7)	15 (12.6)
	North east	39 (7.6)	15 (12.6)
	South west	129 (25.3)	18 (15.1)
	North central	70 (13.7)	19 (16.0)
	South east	103 (20.2)	24 (20.2)
	North west	84 (16.5)	28 (23.5)
History of glaucoma$^{\alpha}$	Not known glaucoma	490 (96.1)	101 (84.9)
	Known glaucoma	20 (3.9)	18 (15.1)
Biophysical factors			
Blood pressure (mmHg) <140/90	Normal	374 (73.6)	65 (55.6)
≥140/90	Hypertension	134 (26.4)	52 (44.4)
Random blood glucose <11.1	Normal	84 (96.5)	21 (95.5)
(mmol/L) ≥11.1	Diabetes	3 (3.5)	1 (4.5)
Body mass index (kg/m^2) 18.5-24.9	Normal	303 (60.5)	71 (61.2)
<18.5	Underweight	76 (15.2)	21 (18.1)
25.0-29.9	Overweight	81 (16.1)	21 (18.1)
≥30.0	Obese	41 (8.2)	3 (2.6)
Glaucoma surgery	Trabeculectomy	12 (2.4)	7 (5.9)
	No surgery	498 (97.6)	112 (94.1)
Type of glaucoma	OAG	360 (91.8)	102 (91.9)
	ACG	32 (8.2)	9 (8.1)

Table 3. Univariate and Multivariate Analysis of Risk Factors for Blindness Among Participants With Glaucoma: Socio-Demographic Factors

		n (%) [95%CI]	**Univariate analysis**			**Multivariate analysis**			
			Odds Ratio	95%CI	p-value	Odds Ratio	95%CI	p-value	VIF
Blind persons		119 (18.9)[15.9-22.4]							
Age (years)	(Min 40)		1.00			1.00			1.46
	Increasing age		1.03	1.01-1.05	<0.001	0.99	0.96-1.02	0.48	
Sex	Female	43 (13.8)	1.00	Reference		1.00	Reference		1.95
	Male	76 (23.9)	1.96	1.30-2.96	0.001	4.59	1.73-12.16	0.002	
Ethnic group	Yoruba	15 (10.2)	1.00	Reference		1.00	Reference		1.06
	Igbo	30 (21.1)	2.36	1.21-4.60	0.01	2.79	1.03-7.57	0.04	
	Hausa	24 (21.8)	2.46	1.22-4.95	0.01	2.69	0.89-8.14	0.08	
	Fulani	10 (38.5)	5.50	2.12-14.28	<0.001	9.75	2.91-32.67	<0.001	
	Kanuri	4 (25.0)	2.93	0.84-10.26	0.09	2.83	0.62-13.00	0.18	
	Ijaw	5 (33.3)	4.40	1.33-14.61	0.02	15.02	1.17-193.69	0.04	
	Ibibio	2 (18.2)	1.96	0.39-9.92	0.42	2.43	0.29-20.36	0.41	
	Nupe	2 (20.0)	2.20	0.43-11.34	0.35	3.22	0.41-25.02	0.26	
	Tiv	3 (27.3)	3.30	0.79-13.81	0.10	7.92	1.65-37.99	0.01	
	Others	24 (18.5)	1.99	1.00-3.99	0.52	4.01	1.41-11.43	0.01	
Marital status	Married	76 (17.6)	1.00	Reference		1.00	Reference		1.57
	Unmarried	43 (21.7)	1.30	0.85-1.97	0.23	2.50	1.03-6.07	0.04	
Literacy	Literate	41 (18.4)	1.00	Reference		1.00	Reference		1.43
	Non-literate	78 (19.2)	1.06	0.69-1.61	0.80	1.03	0.49-2.19	0.08	
Socioeconomic Status	Affluent	17 (11.0)	1.00	Reference		1.00	Reference		1.20
	Medium	20 (9.4)	0.85	0.43-1.67	0.63	0.50	0.17-1.49	0.21	
	Deprived	82 (31.3)	3.70	2.10-6.53	<0.001	3.57	1.46-8.72	0.005	
Residence	Urban	30 (20.6)	1.00	Reference		1.00	Reference		1.08
	Rural	89 (18.4)	0.87	0.55-1.39	0.57	1.48	0.65-3.37	0.36	
Geopolitical zone	North-east	15 (27.8)	2.18	0.97-4.90	0.06	2.18	0.59-7.97	0.24	
	North-west	28 (25.0)	1.89	0.94-3.79	0.07	1.60	0.53-4.86	0.40	
	North-central	19 (21.4)	1.54	0.73-3.25	0.26	1.07	0.38-3.01	0.90	
	South-south	15 (15.0)		Reference		1.0	Reference		
	South-east	24 (18.9)	1.32	0.65-2.68	0.44	0.87	0.30-2.56	0.80	
	South-west	18 (12.2)	0.79	0.38-1.66	0.53	0.54	0.17-1.67	0.28	
History of glaucoma	Not known	101 (17.1)	1.00	Reference		1.00			1.32
	Known glaucoma	18 (47.4)	4.37	2.23-8.55	<0.001	5.89	1.79-19.40	0.004	

VIF = variance inflation factor for covariates in the main multiple logistic regression model; mean VIF = 1.28

Table 4. Univariate and multivariate analysis of risk factors for blindness amongst participants with glaucoma: Biophysical factors

		n (%) [95%CI]	**Univariate analysis**			**Multivariate analysis**			
			Odds Ratio	95%CI	p-value	Odds Ratio	95%CI	p-value	VIF
Hypertension mmHg									
<140/90	Normal	65 (14.8)	1.00	Reference		NI			
≥140/90	Hypertension	52 (28.0)	2.23	1.47-3.38	<0.001				
Blood pressure mmHg	(severity)								
<140/90	Normal	65 (14.8)	1.00	Reference		1.00			1.03
>140/90 – 160/100	stage 1 mild	24 (25.0	1.92	1.13-3.27	0.02	2.29	1.02-5.14	0.04	
≥160/90 – 180/110	stage 2 moderate	15 (27.8)	2.21	1.15-4.25	0.02	1.59	0.64-3.93	0.32	
≥180/100	stage 3 severe	13 (36.1)	3.25	1.57-6.75	0.002	3.53	1.25-9.98	0.02	
Random blood glucose	mmol/L								
<11.1	Normal	21 (20.0)	1.00	Reference		NI			
≥11.1	Diabetes	1 (25.0)	1.33	0.13-13.62	0.81				
Body mass index kg/m^2	(Categories)								
18.5-24.9	Normal	71 (19.0)	1.00	Reference		1.00			1.08
<18.5	Underweight	21 (21.7)	1.18	0.68-2.04	0.56	0.73	0.34-1.54	0.40	
25.0-29.9	Overweight	21 (20.6)	1.11	0.64-1.91	0.72	0.90	0.40-2.01	0.80	
≥30.0	Obese	3 (6.8)	0.31	0.09-1.04	0.06	0.49	0.09-2.62	0.41	

NI = not included in multivariable models.

Table 5. Univariate and multivariate analysis of risk factors for blindness amongst participants with glaucoma: Ocular factors

		n (%) [95%CI]	**Univariate analysis**			**Multivariate analysis**			
			Odds Ratio	95%CI	p-value	Odds Ratio	95%CI	p-value	VIF
Axial length (mm)	(Min 18)	-	1.00			1.00			1.19
	(Max 30)	-	1.15	0.92-1.43	0.22	0.79	0.56-1.11	0.18	
IOP (mmHg)	(Min 5)	-	1.00			1.00			1.09
(higher)	(Max 50)	-	1.06	1.04-1.08	<0.001	1.07	1.04-1.09	<0.001	
MOPP (mmHg)	(Min 6)	-	1.00			1.00			
	(Max 115)	-	0.99	0.97-1.00	0.10	0.99	0.97-1.00	0.14	
Lens opacity	Clear lens	31 (9.9)	1.00			1.00			1.22
	Lens opacity	88 (27.9)	2.72	1.89-3.91	<0.001	1.36	0.78-2.35	0.28	
Type of glaucoma	OAG	102 (22.1)	1.00			1.00			
	ACG	9 (22.0)	1.38	0.69-2.77	0.36	0.63	0.21-1.92	0.42	
Glaucoma surgery	No surgery	112 (18.4)	1.00			1.00			1.23
	Trabeculectomy	7 (36.8)	1.45	0.55-3.96	0.44	0.41	0.09-1.83	0.25	

IOP = intraocular pressure; MOPP = mean ocular perfusion pressure; OAG = open-angle glaucoma; ACG = angle-closure glaucoma.

Table 6. Association of Ocular Factors with Glaucoma Blind Eyes

			For blind eyes					
			Univariate analysis			**Multivariate analysis**		
			Odds Ratio	95%CI	p-value	Odds Ratio	95%CI	p-value
Eyes with glaucoma	Not blind	**Blind**						
N = 890 eyes (100%)	567 (63.7%)	323 (36.3%)						
Ocular factors*								
Axial length (mm) Mean±SD	22.68±0.87	22.89±1.28						
(Min 19.32)	Min 20.42	Min 19.45	1.00			Reference		
(Max 29.92)	Max 25.14	Max 29.92	1.21	1.05-1.40	0.01	1.03	0.81-1.32	0.80
IOP (mmHg) Mean±SD	20±9	28±13						
(Min 5)			1.00			Reference		
(Max 50)			1.08	1.06-1.09	<0.001	1.09	1.05-1.13	<0.001
MOPP (mmHg) Mean±SD	50±15	44±17						
(Min 6)			1.00			Reference		
(Max 98)			0.98	1.06-1.09	<0.001	1.00	0.98-1.04	0.77
Lens opacity								
Clear lens	358 (75.4)	117 (24.6)	1.00			Reference		
Lens opacity	209 (50.4)	206 (49.6)	3.02	2.27-4.01	<0.001	2.13	1.36-3.33	0.001
Type of glaucoma@								
OAG	423 (62.0)	259 (38.0)	1.00			Reference		
ACG	24 (36.4)	42 (63.6)	2.86	1.69-4.83	<0.001	1.25	0.59-2.67	0.56
Glaucoma surgery@								
No surgery	553 (64.1)	310 (35.9)	1.00			Reference		
Trabeculectomy	14 (51.9)	13 (48.2)	1.66	0.77-3.57	0.20	0.71	0.20-2.52	0.60

*analysis adjusted for within person correlation; SD = standard deviation; IOP = intraocular pressure; MOPP = mean ocular perfusion pressure; @ = missing data excluded; OAG = open-angle glaucoma; ACG = angle-closure glaucoma.

Table 7. Relative Risk Ratios of the Glaucoma Outcomes (Glaucoma Not-blind and Glaucoma Blind) Compared to the Non-glaucoma Group

	Frequency distribution (%)			**Relative Risk Ratio (RRR)**						Effect on predicting glaucoma outcome. p<0.05 if the effect is different on the 2 outcomes
	Non-glaucoma N (%)	Glaucoma not blind N (%)	Glaucoma blind N (%)	Glaucoma not-blind			Glaucoma blind			
				RRR	95%CI	p-value	RRR	95%CI	p-value	
Total	12909 (94.98)	546 (4.02)	136 (1.00)							
Socio-demographic factor										
Age-group (years)										
50-59	3447 (96.37)	112 (3.13)	18 (0.50)	1.85	1.37-248	<0.001	1.77	0.85-3.70	0.13	
60-69	2595 (93.58)	147 (5.30)	31 (1.12)	3.13	2.34-4.20	<0.001	3.51	1.77-6.99	<0.001	
70-79	1475 (89.23)	134 (8.11)	44 (2.66)	5.10	3.73-6.99	<0.001	7.43	3.75-14.71	<0.001	
80+	596 (85.26)	72 (10.30)	31 (4.43)	6.69	4.63-9.67	<0.001	10.08	4.85-20.93	<0.001	
Male	5892 (94.33)	267 (4.27)	87 (1.39)	1.15	0.92-1.42	0.23	3.00	1.87-4.83	<0.001	
Ethnic groups										
Igbo	1769 (92.23)	116 (6.05)	33 (1.72)	1.18	0.91-1.54	0.21	3.71	2.01-6.85	<0.001	<0.001
Hausa	3245 (96.15)	97 (2.87)	33 (0.98)	0.62	0.48-0.81	0.001	1.94	1.05-3.56	0.03	<0.001
Fulani	810 (96.43)	18 (2.14)	12 (1.43)	0.47	0.29-0.78	0.003	2.39	1.11-5.14	0.03	<0.001
Ibibio	200 (94.34)	10 (4.72)	2 (0.94)	1.14	0.59-2.23	0.70	2.30	0.51-10.47	0.28	0.40
Unmarried	2619 (92.51)	164 (5.79)	48 (1.70)	1.05	0.82-1.33	0.71	1.85	1.14-3.00	0.01	
Deprived	4191 (93.44)	199 (4.44)	95 (2.12)	0.94	0.73-1.21	0.63	4.42	2.50-7.80	<0.001	<0.001

Chapter 10

Ophthalmologists' practice patterns and challenges in achieving optimal management for glaucoma in Nigeria

Results from a nationwide survey

In discussion with the President of the Nigeria Glaucoma Society

Research paper investigating how ophthalmologists manage glaucoma and the constraints they face

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Student	Fatima Kyari
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Thesis Title	Evidence for improving services for glaucoma in Nigeria

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For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conceived the study. I collected the data. I performed the statistical analyses. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors.

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Ophthalmologists' practice patterns and challenges in achieving optimal management for glaucoma in Nigeria: results from a nationwide survey

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ABSTRACT

Purpose of the study: Glaucoma, a chronic non-communicable disease, and leading cause of irreversible blindness worldwide is a public health problem in Nigeria, with a prevalence of 5.02% in people aged ≥40 years. The purpose of this nationwide survey was to assess Nigerian ophthalmologists' practice patterns and their constraints in managing glaucoma.

Study design: Ophthalmologists were sent a semistructured questionnaire on how they manage glaucoma, their training in glaucoma care, where they practice, their access to equipment for diagnosis and treatment, whether they use protocols and the challenges they face in managing patients with glaucoma.

Results: 153/250 ophthalmologists in 80 centres completed questionnaires. Although 79% felt their training was excellent or good, 46% needed more training in glaucoma diagnosis and surgery. All had ophthalmoscopes, 93% had access to applanation tonometers, 81% to visual field analysers and 29% to laser machines (in 19 centres). 3 ophthalmologists had only ophthalmoscopes and schiøtz tonometers. For 85%, a glaucomatous optic disc was the most important feature that would prompt glaucoma work-up. Only 56% routinely performed gonioscopy and 61% used slit-lamp stereoscopic biomicroscopy for disc assessment. Trabeculectomy (with/without antimetabolites) was the only glaucoma surgery performed with one mention of canaloplasty. Poor compliance with medical treatment (78%) and low acceptance of surgery (71%) were their greatest challenges.

Conclusions: This study indicates that a systems-oriented approach is required to enhance ophthalmologist's capability for glaucoma care. Strategies to improve glaucoma management include strengthening poorly equipped centres including provision of lasers and training, and improving patients' awareness and education on glaucoma.

Strengths and limitations of this study

- This study is the first of its kind, giving insight into available skills, distribution, productivity and training of ophthalmologists in glaucoma care in Nigeria.
- Ophthalmologists from across the country and different healthcare sectors were represented.
- It was difficult to obtain a comprehensive list of all practising ophthalmologists as some are qualified overseas and not all are registered with the Ophthalmological Society of Nigeria (OSN).
- If non-responding ophthalmologists had less access to equipment for diagnosis and treatment, then the equipment available and surgical output may have been overestimated.
- Another limitation is that the study relied on recall by the respondents.

INTRODUCTION

Glaucoma, a chronic non-communicable disease that leads to progressive damage to the optic disc with loss of visual field, is the leading cause of irreversible blindness worldwide. Blindness from glaucoma is avoidable with early diagnosis and appropriate sustained life-long treatment. The number of people (aged 40–80 years) with glaucoma will increase to 111.8 million by 2040, disproportionately affecting people in Africa.[1] The Nigeria National Blindness and Visual Impairment Survey showed a high prevalence of glaucoma (5.02%, 95% CI 4.60% to 5.47%) among adults ≥40 years. One in 5 persons with glaucoma was blind and only 1 in 20 had been diagnosed with glaucoma prior to the survey, suggesting poor knowledge of glaucoma and poor access to services for glaucoma care.[2]

People still go blind from glaucoma in Africa as it is frequently undiagnosed, inadequately treated with poor compliance to treatment regimens;[3] due to limited equipment and treatment options, the high cost of care and lack of awareness among patients.[4–8] Up to 42% of patients with glaucoma attending hospitals in Nigeria are already blind at the time of diagnosis,[9–15] and middle-income earners spend up to 50% of their monthly income on medical therapy for glaucoma which equates to total monthly income among low-income earners.[16]

In order to prevent blindness from glaucoma in Africa, recent advances in technology for diagnosing glaucoma need to be embraced, together with therapeutic options that are effective, affordable and acceptable, combined with ongoing monitoring which can decrease the risk of blindness.[17]

The term physician's practice pattern describes the pattern of practice by doctors to diagnose and formulate a plan of care, in this case by ophthalmologists for glaucoma, within their scope of professional practice.[18] It is defined as patterns of practice related to diagnosis and treatment as especially influenced by the cost of the service requested and provided.[19] Benchmarking practice patterns according to recommended guidelines has important implications for quality of care.

The UK's guidelines (the National Institute for Health and Care Excellence, NICE) recommend that glaucoma be diagnosed using applanation tonometry to measure intraocular pressure (IOP), measurement of central corneal thickness, assessment of anterior chamber angle, visual fields analysis and optic nerve head (ONH) assessment with dilation, using slit-lamp biomicroscopy with a condensing lens (Hruby lens or+60/78/90 dioptres).[20] The NICE diagnostic protocol is similar to recommendations by the International Council of Ophthalmology (ICO)[21] and the American Academy of Ophthalmology (AAO).[22] ICO also recommends documentation of ONH morphology and retinal nerve fibre assessment with colour stereophotography or computer-based image analysis.

NICE recommend a prostaglandin analogue (PGA) or a β-blocker as first-line topical treatment. Surgery with antimetabolites is reserved for those at risk of vision loss despite medical treatment. However, in Africa, one-off procedures such as surgery or laser treatment are recommended due to low compliance with topical medication and the ongoing out-of-pocket expenditure this entails.[9 16] The economic burden on the patient is influenced by the lifetime nature of the treatment as well as the cost of medications.

This study was undertaken to explore current practice patterns of glaucoma care by ophthalmologists in Nigeria and to identify what glaucoma treatments are available and how much they cost. The paper describes management of glaucoma only in patients who come to health facilities where there is an ophthalmologist. We discuss ophthalmologists' practice patterns using the systems thinking concept to try to understand how care provision can be influenced by linkages and interactions between the six components of the health system.[23] The information obtained will be disseminated to ophthalmologists and also used for advocacy to hospital managers and policymakers. The systems thinking approach provides new opportunities to understand processes and enable shared development of interventions[24] by these groups to improve services for glaucoma care.

METHODS

Between September 2010 and July 2012, information sheets for consent to participate and semistructured questionnaires with a space for comments were delivered to ∼250 Nigerian ophthalmologists listed in the databases of the Ophthalmological Society of Nigeria (OSN) and the West African College of Surgeons (WACS). Distribution was to all ophthalmologists participating at the 2010 OSN conference and subsequently by email and phone interviews for initial non-responders and also those not attending the 2010 OSN conference. These avenues for data collection were used for convenient access to ophthalmologists. There were no financial incentives to participate, which was encouraged by reminder emails and telephone calls. Confidentiality and anonymity of responses were maintained.

Information was obtained regarding providers' patterns of care provision. Ophthalmologists were asked about their training/professional background, facility/hospital of practice, availability of functional equipment, and their protocol for glaucoma diagnosis and treatment. Data were collected at individual level as some ophthalmologists worked in more than one facility. They were asked what they considered to be optimum treatment under ideal circumstances, and how they managed their last 10 patients with glaucoma. They were asked to provide information on the number of glaucoma surgeries and cataract surgeries they perform in an average 3-month period, to estimate the ratio of glaucoma-to-cataract surgeries, and to recall surgical complications in relation to use of antimetabolites. Other questions covered systems-related issues such as the cost and availability of glaucoma medication and surgery in their facility, and challenges they faced in glaucoma management.

Descriptive analysis was undertaken using Stata V.14.0 (Stata Corp, College Station, Texas, USA). The distribution of ophthalmologists by healthcare geopolitical zones and states was determined but the findings are reported nationally. Missing data were excluded.

Ethical approval was obtained from the London School of Hygiene and Tropical Medicine and the Federal Ministry of Health, Nigeria.

RESULTS

A total of 153/250 ophthalmologists from 80 centres returned questionnaires (61% response rate). Out of these, 72 (47%) were completed by respondents at the 2010 OSN conference, while the rest were completed and returned by email or by phone.

Demographic details and training background of ophthalmologists

Respondents were aged 34–68 years (median 46 years), 43% were female and the highest number (48; 32%)

practised in the south-west (SW) zone where Lagos is situated (figure 1). All ophthalmologists were based in cities, with 50% in Lagos, Abuja, Kaduna and Ibadan, which also have training institutions.

A high proportion (87%) of respondents had fellowship training in ophthalmology. The number of years since qualification was 1–38 years. Training in glaucoma management was reported as good (62%), fair (18%) and excellent (17%). Thirty-eight per cent had undergone subspecialty training, being higher among those who qualified more than 16 years ago. Ten (7%) had subspecialty training in glaucoma.

The majority of respondents (97%) engaged in continuous medical education (CME) with 87/118 (74%) and 116/138 (84%) attending three or more courses or conferences, respectively, in the previous 3 years. Other sources of CME were online educational resources and medical journals.

Ophthalmology practice

Ophthalmologists practised in government hospitals (63%), private practice (28%), non-governmental/mission hospitals (6%) and military hospitals (3%). About half (75/145; 52%) practised in teaching/tertiary institutions and 33/145 (23%) in state government hospitals. Half (75/150; 50%) said their hospitals ran subspecialty clinics, the most frequent being for glaucoma, paediatric ophthalmology, vitreoretina, oculoplastics, cornea and neuro-ophthalmology.

Most patients (95%) accessed services via walk-in clinics and from community-based outreach screening (73%). Most ophthalmologists (71%) reported that their hospital did not have a written protocol for glaucoma care.

Equipment

Equipment that was available/functional/used in glaucoma management is indicated in table 1. Three ophthalmologists had access to only ophthalmoscopes and schiøtz tonometers.

Service delivery of glaucoma care

Examination and diagnosis

Ophthalmologists saw 3–200 new patients with glaucoma over a 3-month period, with an average of 43 per doctor (SD 37). The most important clinical feature that would prompt a glaucoma work-up was suspicious ONH morphology (85% of respondents) and 7% indicated IOP.

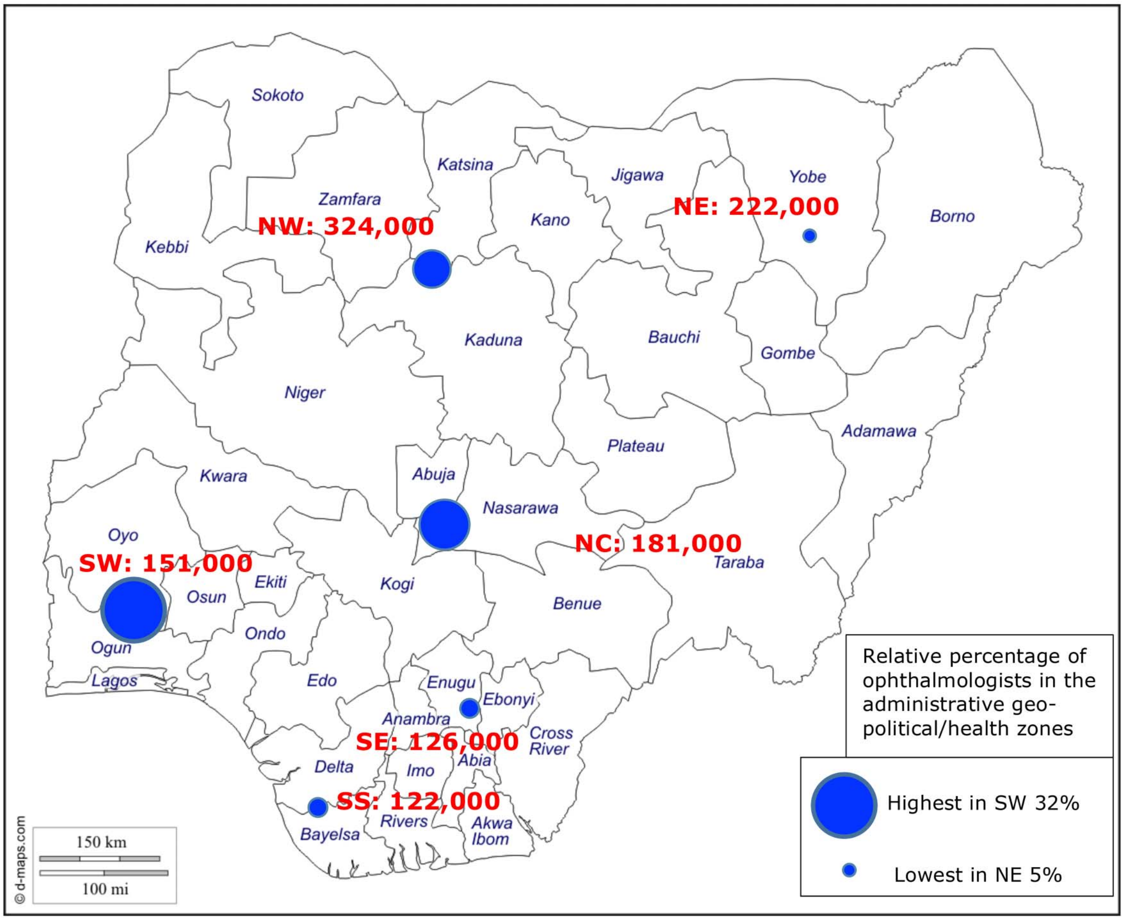

Figure 1 Map of Nigeria showing the magnitude of blindness and distribution of responding ophthalmologists in the six geopolitical zones. NC, north-central; NE, north-east; NW, north-west; SE, south-east; SS, south-south; SW, south-west.

Table 1 Equipment available and used for glaucoma diagnosis and care

Equipment	Available n (%)	Used n (%)	Remarks per cent is of N=146
Ophthalmoscope	152 (99)	142 (93)	
Applanation tonometer	142 (93)	127 (83)	
Schiøtz tonometer	107 (70)	39 (25)	
Other tonometer	76 (50)	53 (35)	Non-contact air puff
Gonioscope	130 (85)	101 (66)	
Slit-lamp lens	136 (89)	113 (74)	
Binocular indirect ophthalmoscope	133 (87)	89 (58)	
Visual field analyser	123 (80)	104 (68)	
Fundus camera	70 (46)	50 (33)	
Ultrasound scan	88 (58)	58 (38)	
Optical coherence tomography	41 (27)	30 (20)	In 14 centres
Scanning laser ophthalmoscope	5 (3)	2 (1)	In 1 centre
Laser	44 (29)	23 (15)	In 19 centres
Pachymeter	7 (5)	4 (3)	1 each in 7 centres
HRT II	1 (1)	0 (0)	

HRT, Heidelberg retina tomography.

When asked how they examined patients with glaucoma, 96% performed cup:disc ratio assessment, 94% measured IOP, 88% assessed visual fields and only 56% performed gonioscopy on all patients. Fewer than 20% routinely performed ONH imaging or assessed corneal thickness. For ONH assessment, most ophthalmologists used a direct ophthalmoscope, 61% used slit-lamp biomicroscopy, 14% used a fundus camera and 11% also used optical coherence tomography.

Glaucoma surgery

Among those providing data on their last 10 patients with glaucoma, 54% patients were offered glaucoma surgery, 35% accepted it and 28% actually underwent surgery (ie, approximately half of those offered surgery underwent the procedure). Of the 124 respondents providing data for an average 3-month period, 60 (48%) performed 5 or fewer glaucoma surgeries and 12 (10%) performed ≥15. There was a wide variation in the number of glaucoma surgeries compared with cataract operations. Overall, ~1000 glaucoma surgeries were performed in 3 months compared with ~6500 cataract operations, giving an average ratio of 1:6.5. However, 80% of ophthalmologists had a ratio of at least 1:10.

Trabeculectomy, with/without antimetabolites or releasable sutures, was the only surgery performed for glaucoma in the preceding 3 months, apart from one canaloplasty. Antimetabolites were used by 88% of surgeons. Only 44% of hospital pharmacies provided antimetabolites and some ophthalmologists obtained these agents privately albeit with difficulty.

The main complications following the last 10 trabeculectomies with antimetabolites were ocular hypotony, cystic blebs, thinned/leaking blebs and shallow anterior chambers. Only 24 (18%) reported that they had audited their last 10–50 glaucoma surgeries.

Regarding follow-up, 68% of respondents did not have a standard written follow-up plan: 70% would give an appointment and hope the patient attended; 20% sent reminders by text, phone or email to non-attenders, or home visits were made. First-degree relatives were requested to attend for glaucoma ‘all the time’ by 60% of respondents, and ‘sometimes’ by 34%.

Implications of health financing

Cost of glaucoma treatment

In total, 113/136 (83%) of respondents knew the cost of the medications available in their facility which ranged from 1000 to 50 000 Nigerian Naira (NGN) (approximately £4–£200) for 1 month’s supply, depending on the type/brand). All pharmacological groups of antiglaucoma medication were available and 97% had both β-blockers and PGAs to prescribe. The cost of surgery ranged from NGN2000 to 190 000 (approximately £8–£760) which was sometimes provided free by non-governmental organisations.

Choice of treatment

Ophthalmologists were asked what treatment they would offer patients with glaucoma if all equipment and treatment options were available to them, and if cost was not a barrier. Over half (54%) chose surgery, mostly trabeculectomy with/without antimetabolites which inhibit scarring, while 41% preferred medical therapy with PGAs. Two doctors preferred laser treatment—trabeculoplasty and selective laser trabeculoplasty (SLT). However, most ophthalmologists would modify their choice, or offer a combination of treatment based on risks and benefits, taking account of disease severity at diagnosis (84%), acceptability (75%), availability (54%) and cost (53%). Other considerations included age, access to care and follow-up, compliance to treatment, family history of glaucoma and coexisting conditions.

Challenges in glaucoma care

The challenges in glaucoma care cited by respondents can be categorised into provider-related, patient-related and health systems-related. *Provider-related* challenges included fear of surgical complications, their inability to offer a cure or improve patients’ vision and the uncertainty of postoperative outcomes. Difficulties in postoperative care were also reported. *Patient-related* challenges included poor compliance with medical treatment, low acceptance of glaucoma surgery, poor awareness and understanding of glaucoma, poor access to care, late presentation, and poor compliance with follow-up. *Health systems-related* challenges included lack of equipment and medication, cost of treatment and a need for more training in early glaucoma diagnosis and in glaucoma surgery.

The ophthalmologists made other comments, highlighting their needs and challenges and how they are being addressed.

Provider-related:

> Glaucoma is such a big burden and the challenges posed by its management are enormous in our setting. The uptake of surgery…is low but with the advent of SLT [laser treatment], a lot more are taking up SLT as adjunct in our centre and so far we are recording successes with regards to IOP control.
>
> There is the need for refractive correction before and after surgical intervention.
>
> Another important practice I observe is to request the presence of spouse/next-of-kin in the pre-op counselling sessions. I am never in a hurry to proceed to surgery.

Patient-related:

> Most of our patients present very late and expect treatment.
>
> (There are) issues of patients understanding of disease progression despite surgery.
>
> We have a Glaucoma Patient Club/Association…

Health systems-related:

> We need to look at acceptable ways for screening and case-finding in the communities rather than waiting for them to come with advanced, late stage disease.
>
> Treatment options are limited: drugs—by cost and availability; laser and surgery—by availability and expertise.

Ophthalmologists highlighted their need for further training:

> Major challenges are (few) opportunities for training and retraining in glaucoma management.
>
> All practising ophthalmologists should be trained on how to manage glaucoma well.

Lack of equipment and maintenance were of concern:

> We don't have an operating microscope for trabeculectomy and no perimeter to assess functional damage and progression.
>
> Our major constraint is non-availability of both diagnostic and surgical equipment and instruments.
>
> Essential equipment like field analyser & OCT require technical support that is not available in the country.
>
> There is a need for an articulated national protocol for diagnosis and treatment of glaucoma.

DISCUSSION

This study, which describes ophthalmologists' practice patterns in relation to glaucoma in Nigeria, is the first of its kind, giving insight into available skills, distribution, productivity and training of ophthalmologists in glaucoma care in Nigeria.

This paper focuses on the human resources for glaucoma care from the perspective of the ophthalmologist. Other allied eye health personnel and the team for glaucoma care were not addressed in this survey. In 2011, Nigeria had an estimated 3.2 ophthalmologists per million population which is just below the ophthalmologist-to-population ratio of 4 per million recommended by VISION2020, which will not be achieved by 2020 without additional intervention.[25] However, the overall figure of 3.2 per million masks maldistribution of ophthalmologists within the country, as the north-east is less well served than the SW, and more needs to be done to encourage ophthalmologists to work in the north. The southern city of Lagos has a large number of ophthalmologists, but there is a shortage of allied eye health personnel who play an important role in glaucoma care.[26]

Training in leadership and management is essential as it would support glaucoma services at the hospital.[27] Given the high prevalence of glaucoma blindness, there is a need for competency-based training for early detection, and surgical and laser treatment of glaucoma, so that all ophthalmologists in Nigeria can manage the condition at secondary and tertiary levels, which would enable glaucoma specialists to focus on more complex cases at the tertiary level. In Africa, there is increasing momentum to improve glaucoma care, encapsulated by the resolution of a meeting in Kampala, Uganda, in 2012.[28] Nigeria now has a glaucoma society (Nigeria Glaucoma Society, NGS), and there are subspecialty training initiatives for glaucoma in the region, such as that in Ghana. Clinical fellowships are also offered by ICO and the Commonwealth Eye Health Consortium.

However, current training has not yet translated into written protocols, their use and challenges. The NGS needs to develop national glaucoma guidelines appropriate to the local context, which include minimal essential diagnostic examination procedures and recommendations on primary treatment.

In this study, training in ophthalmology was reported as excellent by 17% and good by 62%. However, it is noteworthy that there was no specific or detailed information on training. It may seem contradictory that there was request for more training in glaucoma care by some respondents. Young ophthalmologists need to be encouraged to develop competencies in glaucoma early in their careers, with self-audit being an integral component of the training. Prospective monitoring is also essential and can gauge surgical competencies and outcomes.

Ophthalmologists in our study reported high levels of CME. Free online access to journals, such as that provided by the WHO HINARI programme, ONE Network and African Journals Online (AJOL) platforms, is immensely useful as most training institutions or hospitals do not prioritise journal subscriptions.

In our study, service delivery in relation to the management of glaucoma fell short of NICE, ICO and AAO recommendations in several respects, in part due to lack of equipment but also because of late presentation, where visual field assessment is not possible, for example, and low adherence to medical and surgical treatment and follow-up. Similar challenges have been reported in Botswana.[29]

Advocacy will be required with the government to strengthen infrastructure and provide appropriate equipment (with maintenance) in all eye care centres across the country. In this study, ophthalmologists reported that laser was a more acceptable form of treatment than trabeculectomy, and equipment and skills in laser treatment need to be expanded.

Surgery was the treatment of choice in this study, but only about half of patients offered surgery underwent the procedure. Several authors have recommended surgery as first-line treatment for glaucoma in Africa, including in Port-Harcourt where all consecutive patients with glaucoma enrolled in a study were on medical therapy as all had refused surgery. Medical treatment was too expensive for many patients, leading to non-compliance and loss to follow-up.[16] Research is needed on interventions which improve acceptance of surgery, and a randomised control trial of motivational interviewing adapted for glaucoma is currently being undertaken in Nigeria, in which patients are supported to overcome obstacles to accepting surgery or laser.[30] Studies are also required on different forms of laser treatment in Africa. Micropulse diode laser trabeculoplasty has been used with adjunctive effect,[31] and a prospective, observational study of trans-scleral cyclodiode laser photocoagulation as first-line or second-line treatment for patients with advanced glaucoma is ongoing, to assess the effectiveness of these modes of laser treatment which are acceptable and easier to deliver than trabeculoplasty (Abdull MM, personal communication 2015).

Medical therapy with PGAs was the second commonest treatment choice in our study, which were available but expensive. In a hospital study in Benin, there was no significant difference between cost of medication compared with surgical treatment over a 3-year period up to 2008,[32] but this was before PGAs became widely available. Indeed, the clinical outcomes and cost-effectiveness of newer medications versus surgery with antimetabolites is not known.[33] Another trial is taking place in Tanzania, in which SLT is being compared with timolol (Heiko P, personal communication 2015). Audit of outcomes of treatment in black ethnic groups will enable evidence-based choices to be made. Other factors which may improve compliance with medical therapy include policies on marketing, non-branding and cost, and inclusion of PGAs in health insurance schemes.

There was wide variation in the number of glaucoma surgeries reported. The highest number (150 in 3 months) were performed in a high-volume centre where most patients have advanced disease and compliance with medical therapy and follow-up is poor. In this centre, glaucoma surgery is offered to all patients at diagnosis, and performed almost immediately at a highly subsidised cost (respondent, personal communication 2015). The reduced cost seemed to be an important factor contributing to the high volume. Glaucoma surgery needs to be included in universal health coverage and health insurance schemes.

In our study, poor follow-up was a problem. Robust health information systems are important in patient flow and follow-up. Indeed, a hospital study in Benin showed that ≥70% of patients with glaucoma either failed to reattend after diagnosis, or within 9 months. Poor follow-up was associated with worse stage of glaucoma, poorer visual acuity and age.[34] Follow-up may be improved by patient counselling and education, reminders by text, email, phone and community follow-up, and by improving the hospital visit experience for patients.

Patient-related factors contribute to the main challenges of glaucoma care. An important reason for late presentation by patients with glaucoma is lack of awareness about glaucoma.[15] It would be useful to develop a health education pamphlet for the local context, suitable for all including those who are not literate.[27] There is also a need to develop primary-level and community-based case-finding strategies to improve opportunities for early intervention.[35]

A strength of the study is that ophthalmologists from across the country and different healthcare sectors were represented. A limitation of this study was that it was difficult to obtain a comprehensive list of all practising ophthalmologists as some qualified overseas and not all are registered with the OSN. If non-responding ophthalmologists had less access to equipment for diagnosis and treatment, then the equipment available and surgical output may have been overestimated. Another limitation is that the study relied on recall. The eye care team was not addressed in this study.

Further areas of operational research would be the development and investigation of glaucoma care teams involving primary eye care workers for early case detection in the community and other allied eye health personnel for refraction and vision care, counselling, health education and follow-up of glaucoma suspects and patients with glaucoma. This study could also form the baseline to assess the impact on practice patterns following the introduction and dissemination of clinical guidelines.

CONCLUSION

This study indicates that a health systems-oriented approach is required to overcome the major obstacles to providing optimal glaucoma care. Strategies include leadership by the NGS to develop national guidelines and benchmark for service delivery of glaucoma care; infrastructural strengthening for diagnostic and therapeutic/surgical equipment with provision of lasers and training; and medicines. Strategies to improve glaucoma management also include development of healthcare financing strategies through universal health coverage and health insurance schemes; operational/implementation research to develop methods for early diagnosis and robust referral/feedback systems and patients' health information systems.

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Contributors FK led the conception and design of the study, collection, analysis and interpretation of data, drafted the manuscript and edited it with consideration from reviewers' and co-authors' comments. WN contributed to the design of the study and interpretation of data and revised the article for important intellectual content. CG supervised the conception and design of the study, interpreted the data and revised the article for important intellectual content.

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Ophthalmologists' practice patterns and challenges in achieving optimal management for glaucoma in Nigeria: results from a nationwide survey

Fatima Kyari, Winifred Nolan and Clare Gilbert

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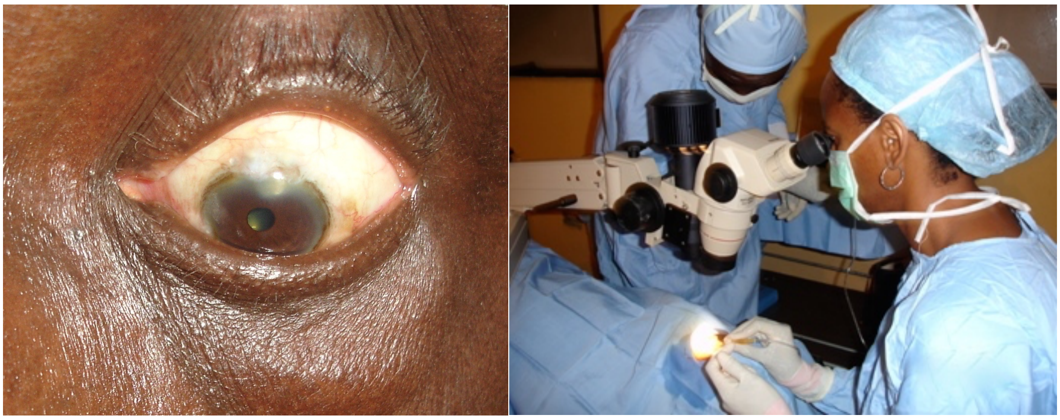
Chapter 11

Managing a patient with open-angle glaucoma: a case study



A filtering bleb with post-trabeculectomy cataract (left); Outreach cataract surgery (right)

Linking material investigating how a panel of expert glaucoma specialists would manage a patient with glaucoma

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SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Community Eye Health Journal		
When was the work published?	February 2013		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
Have you retained the copyright for the work?*	Yes, *see Appendix 7e*	Was the work subject to academic peer review?	Yes

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Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	
Stage of publication	

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I invited the panel for discussion. I collated their responses in intervals as described. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors and discussants.

Student Signature: Kyari **Date:** 28 June 2016

Supervisor Signature: CGilbert **Date:** 30 June 2016

CASE STUDY

Managing a patient with open-angle glaucoma: a case study

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Professor of Ophthalmology, University of Alberta.

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Case presentation

Mr AA is a 48-year-old shop attendant who presented at the eye unit of a teaching hospital with a history of gradual, painless vision loss. His presenting (unaided) visual acuity was counting fingers at 1 metre in the right eye and 6/60 in the left eye. Both corneas were clear, and the pupils had a slow reaction to light. There was a right relative afferent pupillary defect (RAPD). The right eye had a nuclear sclerotic cataract which precluded a good view of the optic nerve head, and a vertical cup:disc ratio (VCDR) of about 0.9, barely visible through the dilated pupil with the binocular indirect ophthalmoscope. The left eye VCDR was 0.8. Intraocular pressure (IOP) was 32 mmHg (right eye) and 30 mmHg (left eye) by applanation tonometry. Gonioscopy showed open angles in both eyes. Visual field tests (standard automated perimetry [SAP]) could not be carried out.

How would the panel manage Mr AA?

Most of the panellists mentioned the importance of talking to Mr AA about glaucoma and what his treatment options were. Some mentioned asking a nurse counsellor to talk to the patient.

The next important issue to be addressed was the setting of a target IOP in the lower teens, and discussing this target with the patient.

There was general agreement that the initial control of IOP should be by medical treatment, while preparing for surgery on the right eye. First choice was a combination of a beta-blocker and a prostaglandin analogue (PGA). A second option was a combination of a beta-blocker and an alpha-agonist. The panel mentioned the need to bear in mind the cost and availability of the drugs.

All panellists agreed that the right eye should be treated first, and firmly recommended a combined procedure: cataract with posterior chamber intraocular lens (PCIOL), and trabeculectomy with adjunctive antimetabolite therapy. The reasons were both clinical and patient related:

"A trabeculectomy alone may give better IOP control, but will likely worsen vision and, depending on the techniques available and how the bleb turns out, going back to take out the cataract could create inflammation and/or directly compromise the bleb and worsen IOP control."

"Cataract surgery alone is out of the picture, since a serious IOP spike could wipe out remaining visual field and adequate IOP control is not likely to be achieved."

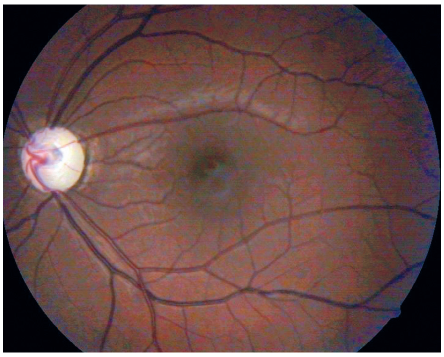
"The patient will better understand the benefit of surgery [and therefore be more likely to attend further appointments] if he can be offered some visual improvement."

Depending on the centre and available facilities, the suggested approaches for surgery on the right eye were:

- phacoemulsification with PCIOL and trabeculectomy
- small incision cataract surgery (SICS) with PCIOL and trabeculectomy at a separate site
- extra-capsular cataract extraction (ECCE) with PCIOL and trabeculectomy.

Adjunct therapy could be with:

- beta irradiation applied with a strontium plaque
- mitomycin C (MMC)
- 5-fluorouracil (5FU).


Fatima Kyari

End-stage glaucoma: disc-cupping

Adjunct therapy is to prevent bleb scarring, however, there is little evidence that MMC or 5FU make any difference in combined procedures.

There is some evidence to support using separate sites rather than the same site in combined phacoemulsification and trabeculectomy surgery.

The choice of treatment for the left eye was not so uniform across the panel. Having initiated medical treatment for IOP control, a top choice was to perform a trabeculectomy with adjunct 5FU or MMC. However, some panellists said they would only offer surgery if there was inadequate IOP control with medications; others would also offer laser treatment as an option.

Both eyes would also have refraction, and the patient would be given spectacles if needed.

Additional comments from panelists

"Patients are becoming more informed and are likely to seek more information and ask for more choices, regardless of their literacy or socioeconomic levels. Therefore, counselling needs to be more comprehensive, to include the biological situation of the eye and whole body, the patient's psychological perceptions, their social and economic situation, as well as their religious beliefs."

"The role of counsellors cannot be overemphasised, as they will take more time to explain to the patient the pros and cons of staying away or declining surgery."

"The nurse counsellor could keep a register with the patient's mobile phone number. She could sms (text) or phone him if he defaults on follow-up."

"When the mode of treatment is certain and options are limited, like in the case of the right eye, then be firm to recommend that to the patient."

Continues overleaf ➤

"In the absence of a visual field test machine, assessment can be done very simply, by confrontation visual field testing, with a red pin or fingers [see page 68]. Some people have abnormally large discs, which may seem to indicate pathology, but have normal visual fields."

"If it is not possible to visualise the disc, for example because of cataract, be guided by the patient's IOP and by the results of visual field tests, however basic."

"It is important to carefully assess for RAPD because the disease is asymmetric. In the absence of any other formal function test (such as visual fields) RAPD is a very useful clinical sign in glaucoma, because it provides objective evidence of functional loss [see page 58]*."*

'The uptake of glaucoma surgery still seems very low in Africa'

Full case and management

After the panelists outlined their management plan for Mr AA, they were given the full case and details of the management that was actually undertaken in his presenting hospital.

Mr AA was diagnosed with glaucoma and cataract at his initial presentation. At that time he was told he had advanced eye disease and needed to have surgery to preserve his vision. He asked whether the operation would make him see better. He was frankly informed that it would only preserve the vision he had at that time in the left eye; and that, if the cataract was causing much of the poor vision in the right eye, his vision in that eye would improve after cataract surgery.

Medical treatment with eye drops (xalatan and timolol) was recommended, and Mr AA was given one month to make a decision about surgery. He was told to get the prescribed medications in the meantime and to start using them.

Mr AA did not return until six months later. He said that he had bought one bottle each of the eye drops, but could not buy more because they were expensive. He decided not to come back to the clinic because he was sure the doctor would be angry with him. At that stage he decided to see a traditional healer on the recommendation of a close family friend.

When this did not work, Mr AA went to a different eye clinic near his home where he was told he had cataract and needed to go to hospital for surgery. This brought him back to the same eye unit, where visual field assessment by confrontation was attempted.

This showed substantial loss of his peripheral visual field: Mr AA was only able to see fingers when they were presented in the centre of his visual axis.

Mr AA was informed that his vision had deteriorated further since the last time he was seen, and that if this continued he would lose vision permanently in both eyes. He was offered combined cataract surgery and trabeculectomy in the right eye, and trabeculectomy only in the left eye. The right eye would be operated on first.

Surgery, rather than medical treatment, was offered because it was clear from past experience that he would not be able to afford to use the more effective eye drops on a regular basis: surgery would be a one-time procedure which would be cheaper for him in the long run.

The decision to offer combined trabeculectomy and cataract surgery was made based on the patient's record of defaulting on follow-up. Removal of the cataract from the right eye would provide him with some improvement in vision as well as IOP control, which would hopefully motivate him to present for trabeculectomy in the left eye at a later time.

Mr AA agreed that he would have the operation this time, but said he wanted time to talk to his family about how they could make the money available. As he could not afford xalatan, he was then asked to use only timolol until the surgery date. Pilocarpine, even though less costly, was not an option for him as cataract surgery was being planned.

Mr AA was given two weeks to make a decision and return.

He returned after three weeks, explaining that the person accompanying him had been away. However, he came prepared to have surgery and was admitted for surgery immediately so as not to lose him.

The standard surgery usually offered at the hospital is manual small-incision sutureless cataract surgery. Mr AA was initially offered right ECCE and PCIOL, because combined SICS and trabeculectomy can be more difficult to perform. However, the final decision was to offer SICS with PCIOL at a temporal site, and simultaneous trabeculectomy with MMC at a more nasal position. The decision to use MMC was to prevent bleb scarring.

Mr AA's immediate post-operative unaided visual acuity in the operated eye was 4/60. He was also informed about the importance of adherence to prescribed medication and follow-up after the operation.

Mr AA returned for his 1-month follow-up appointment and had a post-operative review of the right eye. His unaided visual acuity was 6/60; the bleb was draining and was not cystic; the IOP was 12 mmHg and he was pleased with his improved visual function.

There was some discussion about what to do about the left eye and he was asked to bring his first-degree relatives to the next appointment, so that they could be screened for glaucoma.

Mr AA underwent refraction of the left eye and had a corrected visual acuity of 6/18. IOP was controlled with timolol and xalatan (which Mr AA was able to buy using some of the funds he had set aside for the operation). However, because he expressed concern about not being able to afford life-long medication, left eye trabeculectomy with MMC was subsequently performed.

We are grateful to our reviewers, Clare Gilbert, Richard Wormald, and Nick Astbury for their contributions.

Final comments by the panellists

"An interesting case and very real in our setting. Mr AA highlights the problem that we all experience: non-compliance with topical medication and failure to return for regular follow-up."

"The ophthalmologist made very reasonable decisions in the light of the prevailing circumstances."

"Even challenging situations can lead to success, as seen in this case, at least in the short term."

"Surgery is definitely the right approach in the management of this patient; otherwise the next time he returns his visual acuity may be further reduced."

"The uptake of glaucoma surgery still seems very low in Africa. However, we should realise that, for many of our patients, surgery should be the first line of treatment. Nevertheless, there will still be patients who would adamantly refuse surgery, and for whom we would need to consider laser treatment, if available."

"This case underscores the role of advocacy for universal health care to cover potentially blinding conditions such as glaucoma, as well as the need for greater public education and awareness. These are issues which the ophthalmologist cannot handle alone but which require engagement with government and other community development sectors."

Chapter 12

So let me find my way, whatever it will cost me, rather than leaving myself in darkness

Experiences of glaucoma in Nigeria

Participant discussing at an in-depth interview in his home (top left); a participant signing the consent form for an exit interview in the hospital (top right); some information in this paper was presented, in part, in “Hot Topics: glaucoma” at the Middle East and African Council of Ophthalmology (MEACO 2016) conference, Bahrain (bottom)

Research paper investigating access to glaucoma care and identifying what the community and patients know, do and think about glaucoma

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Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I conceived the study. I collected the data. I transcribed and translated the data. I performed the qualitative data analyses. I wrote the first draft of the manuscript and prepared the subsequent revisions with consideration of comments from co-authors.

Student Signature: ______________________ **Date:** 20 December 2016

Supervisor Signature: ______________________ **Date:** 20 December 2016

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ORIGINAL ARTICLE

So let me find my way, whatever it will cost me, rather than leaving myself in darkness: experiences of glaucoma in Nigeria

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Background: Blindness from glaucoma is associated with socio-economic deprivation, presumed to reflect poor access to care and poor adherence to treatment.

Objectives: To determine why people with glaucoma are presenting late for treatment and to understand access to glaucoma care. Additionally, we sought to identify what patients and the community know, do and think about the condition and why the poor are the most affected with glaucoma blindness.

Design: Study participants were from four communities and two hospitals in Abuja-FCT and Kaduna State, Nigeria. A total of 120 participants were involved, including 8 focus group discussions, 7 in-depth interviews with blind/visually impaired glaucoma patients, 5 rapid direct observation visits with these patients and 13 exit interviews of glaucoma patients in the hospital. The data were analysed using content analysis, interpreting participant experiences in terms of three key steps conceptualised as important in the care pathway: what it takes to know glaucoma, to reach a diagnosis and to access continued care.

Results: This article presents multiple narratives of accessing and maintaining glaucoma care and how people manage and cope with the disease. People may be presenting late due to structural barriers, which include lack of knowledge and awareness about glaucoma and not finding an appropriately equipped health care facility. What keeps glaucoma patients within the care pathway are a good hospital experience; a support structure involving family, counselling and shared patients' experiences; and an informed choice of treatment, as well as agency. The high cost of purchasing care is a major factor for patients dropping out of treatment.

Conclusion: The findings suggest the need to address economic and social structural drivers as glaucoma presents another case study to demonstrate that poverty is a strong driver for blindness. There is also a need for clear glaucoma care pathways with early case finding in the community, two-way referral/feedback systems, well-equipped glaucoma care hospitals and better eye health care financing.

Keywords: *glaucoma*; *blindness*; *vision loss*; *late diagnosis*; *early detection*; *care pathway*; *Nigeria*

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Introduction

Glaucoma is the leading cause of avoidable irreversible blindness globally (1). In Nigeria, the recent national survey of blindness showed the prevalence of glaucoma to be high (5%) among adults aged 40 years and above, 94% of those with glaucoma were undiagnosed and untreated and one in five were blind (2). Poverty and socio-economic deprivation are significant risk factors for blindness from glaucoma (3–5). In a recent study of glaucoma patients in north-eastern Nigeria, 76% were already blind when they presented to the hospital with older age, poor knowledge of glaucoma, rural residence and living more than 10 km from the hospital being associated with blindness at presentation (6). Glaucoma blindness, therefore, reflects disparity in access to care. Additionally, there is a correlation between worsening quality of life and increasing severity of disease (7, 8).

Recent advances in technology for early diagnosis of glaucoma, greater therapeutic options and possibilities for treatment monitoring reduce the probability of

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blindness among patients in the care system in industrialised countries (9). Hence, blindness from glaucoma and the negative impact on quality of life are avoidable. The biomedical description of glaucoma is based on a known set of symptoms and signs including loss of sight, loss of visual field and raised intraocular pressure. Once the diagnosis has been made and the disease named, treatment is recommended to prevent further vision loss and maintain quality of life. Late presentation is when a person presents with biomedically severe/advanced disease in the worse-affected eye where visual acuity is $<3/60$, cup: disc ratio is >0.8 and central visual field is <10 degrees.

In this qualitative study, our main question was why are people with glaucoma presenting late for treatment, with severe/advanced disease, rather than presenting with moderate disease at a point when progression to blindness can be slowed with biomedical intervention. We also sought to identify what patients and the community know, do and think about the condition and why the poor are the most affected with glaucoma blindness. We studied sociocultural contexts that impinge on the delivery of interventions for glaucoma. Providing a critical perspective on services for glaucoma would enable strategies to be developed to deliver more responsive and, hence, effective interventions and care, both for individuals and communities most affected in Nigeria and other sub-Saharan countries with similar high prevalence of glaucoma who also share similar socio-economic and socio-demographic characteristics.

Methods

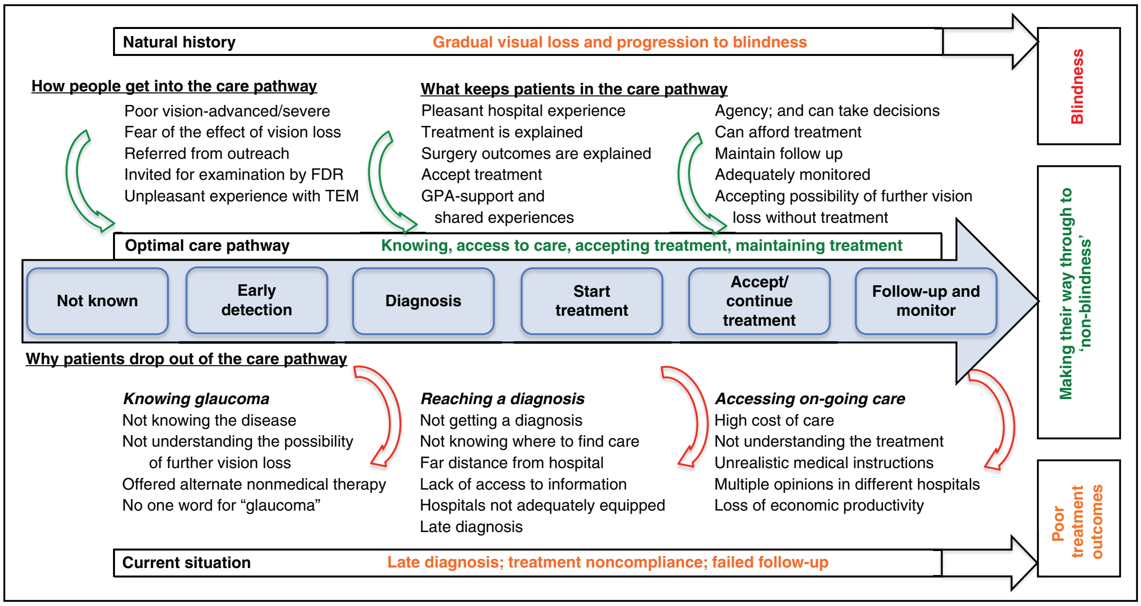
This study employed qualitative methods to assess participants' knowledge and treatment of glaucoma using our clinical perspective as the benchmark.

Conceptual framework

We conceptualised a framework for an optimal glaucoma care pathway (see the central flow in Fig. 1) and imagined that patients should take those steps to avoid blindness. The pathway involved getting to know glaucoma, having a diagnosis, accepting the treatment offered, compliance with treatment and maintaining monitoring and follow-up. In order to obtain data from multiple perspectives, the study employed a number of methods: focus group discussions (FGDs) held in the community, in-depth one-to-one interviews (IDIs) with blind/visually impaired glaucoma patients and their direct observation (DOs), and exit interviews (EIs) of glaucoma patients in the hospital. This range was selected in order to have a wide range of respondents at different sites so as to corroborate findings between people in the community and patients that have accessed care.

Study area

The study areas were Abuja, Federal Capital territory, the capital city of Nigeria situated in the central part of the country; and Kaduna State in the north-west geo-political zone. Abuja comprises six local councils, two of which were included in our study: Bwari and Gwagwalada, in which we included one urban location (Kubwa) and one rural location (Sheda), respectively. In Kaduna, we included one urban location, Tudun Wada, and one rural location, Sabon Birni. Both areas have government and mission hospitals that provide eye care. We selected two hospitals that provide glaucoma services, one in each of the two areas. Hospital 1, located in Gwagwalada, Abuja, is mission-run, and Hospital 2, located in Kaduna, is government-owned.



FDR = first degree relative; TEM = traditional eye medication; GPA = glaucoma patient association

Fig. 1. A conceptual framework for the glaucoma care pathway.

Participant selection and sample size

The study was based on eight FGDs held in the community, seven one-to-one IDIs with blind/visually impaired glaucoma patients, five of whom were directly observed in the community, and 13 EIs of glaucoma patients in the two selected hospitals (Fig. 2), consisting of a total of 120 participants. The fieldwork was conducted between January and March 2012.

The study team consisted of the researcher who is also the first author (FK) of this article, research assistant, also a co-author (MM), and the note-taker/field assistant. The two assistants were trained for data collection in health care research. Training of the assistants by the researcher included a discussion on the overview of the study aim and objectives, procedures, participant recruitment and interview/discussion techniques, and possible challenges and how to overcome them.

Purposive sampling was used to select hospitals and participants. Community-based research facilitators (HR, CO, FE and ES) were involved in selecting the four communities outlined above. The research assistant together with the community-based facilitators, who were involved in community-based rehabilitation of patients with disability or had been on outreach, identified and recruited the participants in the community for the FGDs and the IDIs (and DOs). There were two local ophthalmologists (FA and TN) who facilitated the selection of participants for the EIs in their hospitals. No incentives were provided to participate, but all were offered free eye examination and referral where necessary and refreshments were provided.

Discussions and interviews were conducted in English, Hausa or Pidgin English by FK or MM accompanied by the note-taker, with little need for an interpreter as both interviewers were multilingual in the languages of discussion. However, one FGD and one EI were conducted in Gbagyi where a translator was required. All interviews/discussions were recorded with a digital recording device, and notes were taken.

Focus group discussions

Two FGDs with members of the community were held in each of the four communities, that is, total of eight FGDs, conducting separate discussions for female and male groups in order to have a relaxed atmosphere and foster openness. Participants were aged 30 years and above and included a community leader, visually impaired/blind, and normal-sighted community members. The FGDs were held in a convenient private meeting area within the community. Written informed consent was obtained from participants after explanation of what would take place and their basic demographic data were recorded.

A topic guide was followed in order to stimulate discussion and bring out potential factors exploring the knowledge and practices in relation to eye diseases and blindness in general, and glaucoma in particular, their perception of risks and concept and understanding of blindness. We also explored their health-seeking processes.

After each FGD, the study team reviewed the audio recording, and challenges and need to include more probing questions were discussed.

In-depth interviews

IDIs were conducted with glaucoma patients in the community who were visually impaired or blind and had not accessed treatment or had had treatment whether successful or not. The IDIs were conducted in the participant's home in a place which provided privacy. We carried out IDIs using a narrative approach: 'tell me about your eye problem/disease …' and with a topic guide for prompt questions in order to explore participants' knowledge about their disease, what symptoms triggered them to seek care, difficulties in seeking care, their perception of glaucoma as a cause of blindness and the cost of finding care.

Direct observation

DO involved shadowing the participants to observe how their everyday lives were affected, particularly with regard

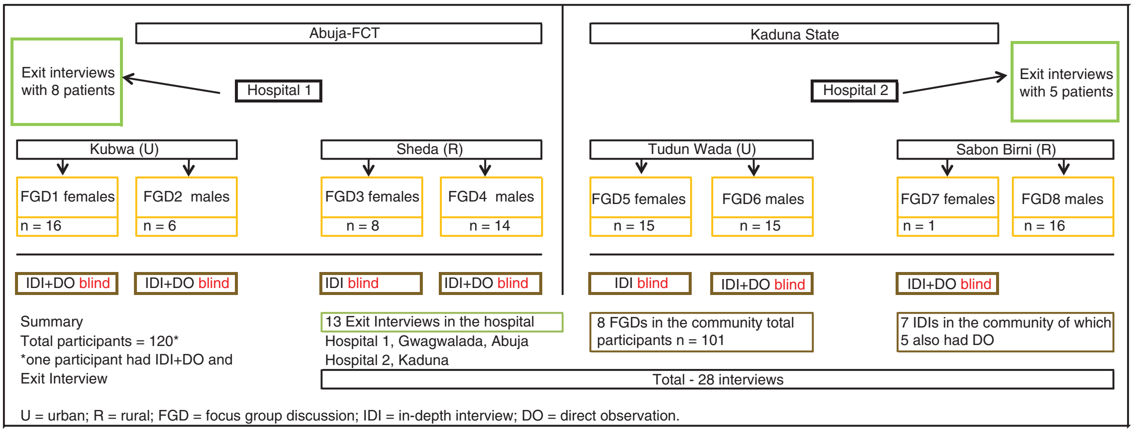


Fig. 2. Sampling strategy and sample size for the patient and community perception study.

to their home environment and interactions within the community. We selected IDI participants who gave us the opportunity to observe them in their homes. We had a checklist of observations, which included how they interacted with their family members and how members of the community approached and related with them. We also observed how independent they were in terms of mobility, use of everyday gadgets such as mobile phones and telling the time.

Exit interviews

One-to-one EIs were conducted, and participants were asked to narrate their experience of the hospital visit and what they felt about the diagnosis and treatment. This also included their positive experiences, rather than only barriers to accessing health care. They were also asked about triggers that led them to seek care, whether their condition was explained to them and what they understood about glaucoma and the effects of their sight loss on their everyday lives, and how much money they had spent on eye care. They were also asked about their knowledge and use of traditional (non-medical) eye medication (TEM) and what they would tell new patients who had been diagnosed with glaucoma. Participants ranged in age from 29 to 74 years.

Data handling and analysis

The audio recordings were transcribed in the language of discussion. Hausa transcripts were translated into English. English translations were crosschecked and finalised by FK. English transcripts of FGDs, IDIs (and DOs) and EIs were imported into NVivo 10 (QSR International Pty Ltd., Victoria, Australia). The data were accessible to only the researcher and co-authors.

Data immersion

The researcher became familiar with the data through conducting, transcribing and translating most of the interviews. Transcripts were read carefully and coded line by line.

The data were analysed using content analysis, interpreting participant experiences in terms of three key steps conceptualised as important in the care pathway: ‘knowing glaucoma’ which gave a perspective of people’s experience and not compared to what they should know; ‘reaching a diagnosis’ which stems from knowing glaucoma and as a prerequisite for treatment; and ‘accessing ongoing glaucoma care’ which includes issues of cost of care, decisions on treatment and non-medical alternatives that people might be offered. Within each step, we identified explanatory themes. The themes were developed based on initial reading through the transcripts. A coding template was set up for the three themes that emerged from the data and agreement of categorisation reached through discussion and review by the co-authors (CC and CG). We remained open to additional codes and new themes that emerged during analysis. Additional codes were applied in order to identify what it really meant to people to have glaucoma and how debilitating it was. Initial coding was done by hand, and subsequent categorisation and archiving were done using NVivo 10 (QSR International).

Ethics

Ethical approval was obtained from the Ethics Committee of the London School of Hygiene and Tropical Medicine, UK, and the Nigeria National Health Research and Ethics Committee. Written informed consent was obtained from the participants. We specifically asked to record interviews, take photos and use anonymous quotes. Confidentiality and anonymity were maintained. The study did not interfere with any treatment that patients were receiving. Participants in need of further management for their eye condition were attended to and referred to the appropriate facility if necessary.

Results

Study participants

All participants in the FGDs ($n = 101$) were aged 30 years and above (Table 1). Basic demographic characteristics of the IDI and EI participants ($n = 19$) are shown in Table 2.

The findings represent narratives of accessing and maintaining glaucoma care and how people managed and coped with the disease. It is important to know that from many people’s perspective, there is no care pathway; it is just life, the lived reality. Thus, other aspects we explored were the coping mechanisms of patients with glaucoma and the consequences of fear of the effect of sight loss, feelings of isolation, abandonment, stigmatisation and loss of autonomy as well as financial stress and loss of economic/social productivity. The coping mechanisms were within sociocultural constructs of faith in God and support from family, friends and community. It was not only about coping with the disease, but also about coping with the social situation they were in.

Some quotes have been paraphrased to ease reading without losing the context and meaning captured in the discussion. Furthermore, four cases are presented to illustrate the different themes.

Knowing glaucoma

Blindness is generally considered a serious problem. However, participants avoided use of the term ‘blindness’ or ‘*makanta*’ (Hausa), rather they would say ‘eye problem’ or ‘*matsalar ido’* (Hausa). Participants’ description of blindness often indicated a total loss of vision, attaching a morbid reality to it, while those with poor vision did not always define themselves as blind.

There was generally poor knowledge of eye diseases as understood in biomedicine and lack of access to information. Most participants got information about health

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Table 1. Demographic characteristics of participants of focus group discussions in the community

	Number of participants (%)		
	Rural (Sheda and Sabon-Birni)	Urban (Kubwa and Tudun-Wada)	Total
Gender			
Female	19 (39)	31 (60)	50 (50)
Male	30 (61)	21 (40)	51 (50)
Age (years)			
30–45	6 (12)	11 (21)	17 (17)
46–60	17 (35)	17 (33)	34 (34)
61 and older	4 (8)	22 (42)	26 (26)
Not indicated	22 (45)	2 (4)	24 (24)
Occupation (current/retired)			
Civil service officer	–	6 (12)	6 (6)
Driver	–	2 (4)	2 (2)
Farmer	9 (18)	1 (2)	10 (10)
Housewife	6 (12)	16 (31)	22 (22)
Military	–	1 (2)	1 (1)
Office assistant/ cleaner	1 (2)	3 (6)	4 (4)
Student	–	1 (2)	1 (1)
Teacher/lecturer	2 (4)	3 (6)	5 (5)
Trader/business	3 (6)	16 (31)	19 (19)
Not indicated	28 (57)	3 (6)	31 (31)
Total participants	49 (100)	52 (100)	101 (100)
Language of discussion			
English	–	2 (50)	2 (25)
Gbagyi[a]	1 (25)	–	1 (12.5)
Hausa	3 (75)	2 (50)	5 (62.5)
Total FGDs	4 (100)	4 (100)	8 (100)

FGD, focus group discussion.

[a] An interpreter was used in this FGD.

issues from the radio. Other sources are places of worship (church and mosque), through reading and interaction with neighbours or health workers. They, however, would rely on information given them by the doctor or at the hospital during health talks. They described symptoms without giving specific names for eye disease except for cataract (*yana*) and corneal opacity (*hakiya*), though sometimes they interchanged description of the two. Most participants had not heard about glaucoma, and they recognised that self-medication with inappropriate medicines would cause delay in seeking treatment.

None of the patients had heard of the term ‘glaucoma’ before their diagnosis. They did not bundle their symptoms and experiences as a disease entity, and there was no reference to any biomedical category. Some of their symptoms such as redness and tearing were often considered to be common and less sight-threatening eye conditions. Different things happened over time, such that by the time they sought treatment, there was severe vision loss in at least one eye. Participant EI-8 said ‘I cannot see very well. Like I am in the dark’, and EI-4 felt indeed glaucoma is a *silent thief of sight*.

People’s experiences differed, and some participants came to know things were not quite right with their vision, some of which may indicate visual field loss. For example, not being able to see the right underarm while shaving was illuminating for EI-1, whereas EI-13 could only see clearly through the corner of the eye, and IDI-7 could not see people’s body completely.

Factors related to *not* knowing glaucoma included stigma around blindness and poor vision so that they would not talk about it; misconceptions on causations of eye diseases; and general lack of awareness, knowledge and access to information about glaucoma and eye diseases. These factors led many participants in the care system to present with late disease and to access multiple opinions in different hospitals, *hopping and hoping*.

Reaching a diagnosis

Knowing glaucoma is part of reaching a diagnosis. Even when they got to know they have glaucoma, some have no information on what to do about it. In health care centres where there are no trained health-workers or appropriate equipment, then one cannot make a diagnosis of glaucoma. Participants did not have a designated entry point into clinical care, and there was no system of referral. Participants did not know where to find care or what treatment to expect nor did they appreciate the possibility of future sight loss without treatment, which led some to visit multiple providers – going from one health facility to another. As IDI-5 experienced: ‘I kept going (to the hospital). Then, the hospital was moved to Shika. Then I started going to Eye centre. Thereafter I went to Dan Tsoho. I was n’t satisfied, so I went to Zaria. Then I was told that there was a hospital in Kano. I started going there. I was not comfortable so I changed to another hospital, right there at Kano’.

The high cost of finding care contributed to these difficulties, but EI-11 had agency and was determined to find and maintain care (Box 1). On the contrary, inability to make autonomous decisions for one’s own benefit contributed to delays in making a diagnosis (see Box 2: IDI-2). Some participants mentioned distance to hospital was a reason for their poor access to care and felt they had no bargaining power and could not request for services to be brought closer to them.

Thus, the contributory factors for late diagnosis include poor knowledge about the disease, not finding an appropriately equipped hospital and inability to afford care.

Table 2. Basic demographic information for the participants who had in-depth interviews in the community and exit interviews in the two selected hospitals

No.	Code	Gender	Age[a] (years)	Occupation	Available clinical description
1	IDI-1; EI-2	F	62	Housewife (military)	VA: RE 6/9, LE HM; BE CDR 0.9
2	IDI-2	M	60	Retired as military nurse	VA: NPL BE; BE CDR 1.0
3	IDI-3	M	59	Stopped driving	VA: NPL BE
4	IDI-4	M	45	Trader	VA: RE PL, LE NPL
5	IDI-5	M	75	Butcher	VA: RE CF, LE 6/9; RE CDR 1.0, LE CDR 0.9; LE trabeculectomy 12 years
6	IDI-6	F	67	Housewife	BE not seeing. Sees some shadows
7	IDI-7	M	43	Teacher	VA: RE NPL, LE NPL; Diagnosed glaucoma and had RE trabeculectomy 9 years ago; then had RE vitrectomy for endophthalmitis 6 years later
8	EI-1	M	29	Works with a trading company	RE not seeing
9	EI-3	M	56	Stopped work	RE cloudy; LE not seeing
10	EI-4	M	52	Senior civil servant (Intelligence department)	Diagnosed glaucoma 8 years ago; Had triple procedure in first eye and trabeculectomy only in second eye
11	EI-5	M	40	Farmer	LE not seeing
12	EI-6	M	74	Lecturer at college of education	One eye blind since early adulthood. Had cataract surgery and diagnosed glaucoma in the only eye
13	EI-7	M	58	Electrician, works with contractor firm	One is bad. Diagnosed glaucoma more than 5 years ago
14	EI-8	M	60	Farmer	RE not seeing clearly; had RE trabeculectomy
15	EI-9	F	53	Theatre nurse	RE worse; had RE trabeculectomy
16	EI-10	M	53	Worked in telecommunications. Made redundant due to company closure	BE seeing ok
17	EI-11	M	42	Vehicle insurance officer (civil servant)	LE not seeing – had surgery in LE prior to diagnosis of glaucoma in BE
18	EI-12	M	70	Dependent on children	RE not seeing
19	EI-13	M	62	Mechanic, contractor	One sees well, other not much

IDI, in-depth interview; EI, exit interview; VA, visual acuity; RE, right eye; LE, left eye; HM, hand motions; BE, both eyes; CDR, cup-to-disc ratio; NPL, no perception of light; PL, perception of light; CF, counting fingers.
[a]Some ages were estimates.

Accessing and maintaining glaucoma care

Hospital experiences varied considerably. However, a good hospital experience and obtaining appropriate information made a difference in patients' understanding of their disease and gave them hope.

Family members are cardinal in decision-making for choice of treatment options, and participants would often discuss with them before taking decisions. Thus, patients and their carers/family need to fully understand the disease and the implications of choices of treatment. Once a diagnosis of glaucoma is made and choice of treatment is considered, physicians need to discuss treatment options with the patient and family. This is also helpful for identifying first-degree relatives with glaucoma. IDI-4's older brother was already blind at the time of diagnosis. IDI-4 also had late diagnosis and could not sustain medical treatment, and he gradually became blind. His younger brother was also diagnosed late but had surgery in the only seeing eye and this helped to maintain his vision.

Some participants had unpleasant experience with TEM (see Box 3: IDI-6).

Hospital charges and cost of medicines were a great concern, and in some cases, these contributed to poor compliance with medical therapy. IDI-4 could not keep up with buying medicines due to cost, and IDI-7 lamented that all he had spent was to no avail. Inability to afford hospital costs precluded patients from getting and maintaining treatment. FGD/4/P6 mentioned 'Actually, in the hospital, they asked me to pay about N60,000 (£240). But with that amount of money requested, I just put the paper in my pocket and went back home. One who has not even N100 (£0.40p) at home, they ask for N60,000 (£240); how can you even begin to get that?' On the contrary, EI-4 alluded to the availability of health insurance as being beneficial for enabling access.

In terms of getting information about their disease, some perceived a hierarchical doctor–patient relationship characterised by one-way communication, with the patient

Box 1. EI-11 illustrates late presentation, getting to know glaucoma, agency, accepting the possibility of further vision loss without treatment and maintaining continued care

EI-11 is a 42-year-old senior civil servant:

When I discovered that I had eye problem . . . one eye was seeing, one eye was not seeing, I said I cannot continue like this, let me find my way to FMC but I was stopped by a friend who recommended a private clinic. I did not know it was run by a nurse. There, I was told I had glaucoma. He did not give much guidelines and explanation. Had I got guidelines and explanation, it would have not reached up to this stage at which I am in now. Later, after one year plus, I changed to a private doctor. He also said I had glaucoma and one of my eyes was severely affected. That is the left eye. Then he explained glaucoma. And ah, that's how I started to know about glaucoma.

Because at the private hospital, . . . you will spend much and much and much and much. I asked him to give me a referral letter to NEC. He said 'why refer if it's what I can do?' Though he's a qualified doctor, he's a doctor. Then I later thought it over . . . I said kai . . . (sigh) I'm educated so let me find my way. Whatever it will cost me, let it cost me rather than leaving myself in darkness. And I don't want to be in the dark!

Here, they explained ALL (his emphasis) things to me. And they said ANY (!) nerves, or ANY (!) eye sight that glaucoma destroys, it is destroyed for life. So that's why I said I cannot stay and continue looking at it . . . then leaving myself in darkness. Because I am still young, I don't know how long I will live in the world and my eye . . . Then that I'm finished. So that's why I normally maintain the period I'm given for appointment. I don't fail it. I don't fail it. Yes.

not having courage to ask for explanations. Some participants felt this was because clinicians have enormous social responsibilities despite their busy work schedule and much is expected from them. Rather, they were satisfied with a one-to-one guidance and counselling on their disease.

Having a forum such as a glaucoma patient association would promote interaction between patients, with representation for actively addressing challenges in accessing care and treatment and obtaining social support. Participants believed that shared experiences would enhance ability to make informed choices and staying in treatment.

What keeps glaucoma patients within the care pathway are a good hospital experience; a support structure involving family, counselling and shared patients' experiences; and an informed choice of treatment, as well as agency – knowing about glaucoma and being able to do something about it. The cost of treatment is a major factor for patients dropping out of treatment.

Box 2. IDI-2 illustrates lack of autonomy to take decisions, not understanding the treatment and feeling of abandonment but accepting the situation he is in

IDI-2 retired as a staff sergeant after 35 years in the military as a nurse. He is blind in both eyes from glaucoma. He is a widower and lives with 3 of his 5 children, the youngest being 11 years old. The oldest son is away on military service, and the oldest daughter is at University. Interviewing him was my second IDI of a blind person in the community.

'When I was diagnosed with glaucoma in 2004', the doctors suggested surgery. However, my preparation for retirement from the military stopped the discussion of surgery. Then things happened so quickly – I was retired, had to leave the barracks official accommodation to my uncompleted house which was yet to be roofed. 'At the time I moved to this place I could see and move around everywhere'. That was 2007.

'At the hospital, I had been receiving treatment but there was no improvement. I went to another hospital'. I continued treatment until I got fed up . . . 'Anywhere I went, they would say timolol, timolol . . .'

When asked about how he copes being blind – 'It is not easy . . . The children would just go away. Not that we don't have . . . I have television, DVD, radio, anything that can make them happy to stay here. I don't shout at them – there's food, everything. I don't know why . . . I'm not having peace of mind again. As I cannot see anything at all how can I go out myself? There is nothing I can do . . . The challenge is too much but there is nothing I can do. What can I do? Do I cry? If I cry, am I the first person to go blind? So there is nothing I can do than to accept it like that. So I have to thank God very well. 'It is said in the Bible that in any situation you see yourself, accept it'.

Having glaucoma and coping mechanisms

IDI-2 expressed feelings of isolation and abandonment and loss of value to his children and friends (see Box 2), while some participants note that their visual impairment should not define who they are. IDI-5 felt awful for being called 'blind-man' (*makaho*). Likewise, IDI-7 who had been active in the community for about 40 years disliked being addressed as 'blind-man' (*makaho*): 'why would people address me as such and alienate me?'

A diagnosis of glaucoma triggered anxiety: EI-1 said, 'I had a breakdown. A shock went through my spine'; or

Box 3. IDI-6 illustrates lack of access to medical care, use of traditional eye medication and not understanding treatment

> IDI-6 is a 67-year-old housewife. Her husband is the District Head. She is blind in both eyes from glaucoma. She has never been to a hospital/clinic nor been on biomedical treatment:
>
> 'My eyes kept hurting and hurting and then they brought me some perfume which I sprayed on the eyes. But they got worse. Then they said I should take a frog and rub it on the eyes. I said I couldn't do that. Then my husband picked up the frog and rubbed it on my eyes and when he threw the frog, it died. The eyes got better, there was no pain again. Then they gave me kohl which I kept applying for months and years and the vision continued dimming and getting worse. Now, that is my story'.
>
> Asked why she didn't go to the hospital –
>
> 'I have not been to hospital. The first time they came (on outreach), I was told I needed operation. But some people said to my husband that if I went, they would sever my eye nerves (*za'a tsinke jijiya*) so I refused to go since then'.

perhaps regarded as a fate worse than death because 'some people prefer to die instead of living with blindness' (EI-4). There was also an emotional component as IDI-1 kept sobbing during the interview while saying 'God, you know better, you will make it better'. Participants who had lost vision expressed their dismay in their inability to do certain tasks especially driving, writing and keeping their jobs. Some also had feelings of being a burden on those who assist them in their everyday activities.

Within the sociocultural framework of faith in God, some glaucoma participants did not see themselves as being blind and now suffering. Rather, they found ways to manage the situation. FGD/4/P3 said 'I put my trust in God' (see also Box 4: IDI-7). IDI-4 remains an important member of his community as the *Imam* who leads the congregation prayers in the local mosque. He finds strength in faith and accepts that everything in life would be left behind anyway.

Discussion

This study found that most people do not know about glaucoma, they are not aware when they have it, they do not know where to find care and they are faced with challenges in accessing and maintaining treatment because of poor infrastructure and high cost of care. A major trigger of seeking care was advanced loss of sight resulting in late diagnosis. Indeed, a person with glaucoma may frequently be unaware of the gradual loss of sight (10, 11). Loss of sight was often not discussed, and participants did not use the word 'blind' (*'makanta'* in Hausa) to describe

Box 4. IDI-7 illustrates late diagnosis, difficulties in maintaining care, poorly equipped tertiary hospital, agency and coping mechanisms

> IDI-7 is a 43-year-old man, civil servant.
>
> 'In 2003, the doctor said my left eye had end-stage glaucoma. I never knew that it was not seeing before I went to the hospital. It was when they tested me that I knew. They recommended surgery for the right eye. I had the first surgery in 2003 and continued to see without any problem. I would go for check-up regularly. Four years later in 2007, my seeing right eye got reddish. I got worried and went to see the ophthalmic nurse who recommended an eye drop. It was not available in my town so I bought it about 30 miles away. I saw my vision diminish gradually . . . The following day I went to NEC. I needed vitrectomy but they didn't have the materials. Through a cumbersome process of referral, appointment and solicitation of funds, I had vitrectomy in Cairo, Egypt, two weeks later'.
>
> 'My work keeps me busy. Currently I am heading a centre that teaches secondary school students English and Mathematics. We recruited 12 lecturers and we have about 6 classes with over 65 students'.
>
> However, he expressed disturbing limitations as a public speaker and teacher. 'You know when I address people, the only response I can hear from them is laughter or their voices, but I cannot see their eyes . . . That is one of my problems. Some people do not talk, but you can read them from their faces. But I cannot read those because I cannot see. It is only when somebody talks that I begin to know his feelings about me, so that is one of the disturbing things'.
>
> 'It has stopped me from furthering my studies, Masters. After the first surgery, I could not read . . . But most importantly, I was not sacked from my job – that is a happy thing. I earn my salary and maintain my family'.
>
> On his relationship with his family and community: 'My family and friends have been very, very supportive. Especially my wife . . . The community too. If people could remove this sickness from me, the number of people that trooped into this house when I came back from hospital, they would have removed the sickness from me, on sympathy basis, I tell you . . . I gave everything to God'.

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themselves. This silence can be seen to have allowed glaucoma to thrive without being diagnosed. As in Ghana (12), there was no specific name for glaucoma in the communities we studied. Similarly, the knowledge of glaucoma was low, as documented in previous hospital-based (13–16) and population-based (17–20) studies. Even in some developed economies, knowledge of glaucoma varies (21, 22). The lack of knowledge might have contributed to difficulty in appreciating the possibility of future sight loss if left untreated even though patients would live with future uncertainties (23). However, it was not only the silent nature of loss of sight due to glaucoma that precluded participants from finding or securing early care but also additional factors such as not knowing where to find care and not being able to afford or sustain care. In a study, where care is available and accessible, every patient followed up in a population-based survey had sought eye care (24), but the understanding of glaucoma was limited (25). In our study, those who had more agency, that is, resources and ability to take autonomous decisions, appeared to have found ways to access care.

In line with the United Nations resolution on Universal Health Coverage (26), a Global Action Plan (GAP) was developed for eye care (27). GAP aims to ensure that the diseases that cause blindness and visual impairment are addressed through universal standards of eye care, tailored according to local contexts and benefits of modern medicine. The GAP, inherently linked with vision 2020 'The Right to Sight' (28), recognises the need to address problems of unequal access to eye care and to support weaker nations/communities to achieve those standards. This study provides information that will be useful to developing strategies for locally relevant eye care tailored towards optimal care.

In interpreting our findings, we identified the concept of structural violence as a useful way to understand and explain what could be causing people to be in the situation of lack of knowledge, late presentation and drop out from continued care. Structural violence originates from the perspectives that there is a disease and that the disease is disabling – for example, HIV/AIDS and there are structures that make the disease worse in others and structural inequalities that prevent access to care (29). When there are constraints and inequalities in socio-economic status and health systems structures, as we note here, that preclude avoidable blindness from being avoided, then there is structural violence (30). Put more succinctly, 'structural violence is one way of describing social arrangements that put individuals and populations in harm's way. The arrangements are structural because they are embedded in the political and economic organization of our social world; they are violent because they cause injury to people (typically, not to those responsible for perpetuating such inequalities) ... neither culture nor pure individual will is at fault; rather, historically given, and often economically driven processes and forces conspire to constrain individual agency. Structural violence is visited upon all those whose social status denies them access to the fruits of scientific and social progress' – Paul Farmer (29, 31). The concept of structural violence encourages us to reorient ourselves towards finding solutions, to critically engage the realities and recognise the situation due to structural inequalities and structural barriers, which cause harm, rather than passively accepting these as systemic inequalities (32). These structures of inequalities are invisible and embedded within the same political and economic systems such that no one individual or institution can be held accountable (31). For example, if a person goes irreversibly blind from glaucoma, which is avoidable, one might ask, who do we hold culpable?

In terms of agency, autonomy is related, partially, to having the ability or the resources to act freely. From the economic aspect, it could mean those who have a voice – for example, EI-11: 'this is what I want', wherein the socio-economic structure enables him. However, when people are unable to demand, the only agency they may have is to lament and leave – for example, IDI-2: 'what else can I do?' For those who had relatively better agency, for example, EI-11, they were able to seek care and navigate the difficult care pathway 'rather than remain in the dark'. That was an active response. A somewhat passive response is accepting the situation and not taking a decision to go for a biomedical or traditional medicine but manage the 'misfortune' (e.g. IDI-6) and readjusting their social and family interactions (33, 34). This may not necessarily be interpreted as social suffering in the way people manage adverse situations, but takes into consideration coping mechanisms. The way they cope and the way they accept their situation might be because of the absence of care or structures that mean they cannot access care and they do not feel or know that getting better care is their right. It appears that health choices have been left to ordinary people to continue their own therapies, be it traditional medicine or self-medication from patent medicine stores or markets. This has been described as 'subsistence' health – where people are left to seek their own care (35), and traditional medicine is often sought where there were no alternative sources of treatment (36). In glaucoma, there is no system, no diagnostic category and no way of well-established management of the disease within traditional medicine. In fact, the more established practice of couching, which is the traditional manual manipulation for cataract, is widely practiced in Nigeria with very poor visual outcomes (37).

Furthermore, the narratives imply that whether one goes to the hospital or gets treated was a matter of fate and destiny, depending on the will of God. In a way, this submission to the will of God breeds acceptance of the situation. Some believe that loss of their sight is a test of their faith and perhaps an expiation of sins for a better life after death. Of note, however, is that coping may be a response to the absence of care or the structures that mean they cannot access care. This makes the coping mechanisms dynamic – people have resources and ability to manage the situation but they would not turn down the opportunity to have better care that is well explained, accessible and affordable.

Limitations

There are limitations of this study. The analysis was undertaken using the transcripts of translation to English for three-quarters of the discussion. As such, some distinct expressions might have been lost in translation. Another limitation is that we conceptualised a care pathway and saw people who are not accessing or who are falling out of our imagined pathway. But from their perspective, there is no care pathway; for them, it is just life, embodied as lived realities. Additionally, a limitation of the structural violence perspective is that it labels one with a defining feature, for example, the glaucoma blind, whereas these patients did not see themselves as such.

Recommendations

This population-based study provides a baseline and deeper understanding of access to glaucoma care. However, we recommend conducting a similar study in different settings for local content. A further recommendation is that in addition to offering biomedical/clinical service, providers need to collaborate and communicate effectively with patients, family members and carers so that they understand the disease, manage their expectations and be effectively supported to gain insight into the disabling consequences of blindness. Other needs are better eye healthcare financing, visual rehabilitation and social adaptations for people with visual impairment/blindness. A social policy and disability benefits would also ease some of the social suffering of blindness.

Conclusion

In Nigeria, the reasons for late presentation imply the need for improving services for glaucoma. Availability and affordability of treatment need to be addressed so that hospitals are well equipped to manage glaucoma, incorporating early case-detection strategies with clear glaucoma care pathways and two-way referral/feedback systems.

Authors’ contributions

FK led the conception and design of the study, collection, analysis and interpretation of data and drafted the manuscript. CC contributed to the design of the study and development of the topic guide, data analysis and interpretation of data. MM contributed to the development of the survey instrument and participated in data collection and interpretation. CG supervised the conception and design of the study, interpreted the data and contributed to manuscript preparation. All authors revised the article for important intellectual content and approved the final version of the manuscript.

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Paper context

Blindness from glaucoma is associated with late presentation and poor compliance to treatment. This study indicates that late diagnosis may be explained by structural barriers to accessing care: socio-economic deprivation, poor understanding of the disease and high cost of care. The findings suggest the need to address socio-economic structural drivers as glaucoma experiences demonstrate that poverty is a strong driver for blindness. There is also a need for clear glaucoma care pathways and better eye healthcare financing.

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Chapter 13

An ideal service for glaucoma would be…


Adun Ogunro

Determining the functional and structural deficit in glaucoma and monitoring of progression/response to treatment: Visual field assessment using frequency-doubling technology (left); Optic nerve head assessment by optical coherence tomography (right)

A perspectives paper proposing a top-down approach to developing glaucoma services

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SECTION A – Student Details

Student	Fatima Kyari
Principal Supervisor	Clare Gilbert
Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

SECTION B – Paper already published

Where was the work published?	Community Eye Health Journal		
When was the work published?	December 2014		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	N/A		
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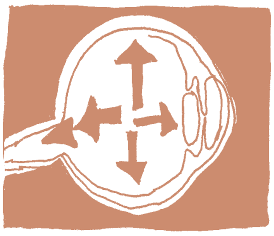
Student Signature: FKyari **Date:** 28 June 2016

Supervisor Signature: CEGilbert **Date:** 30 June 2016



GLAUCOMA SERVICES

'An ideal service for glaucoma would be…'

Fatima Kyari
Ophthalmologist/Senior Lecturer: College of Health Sciences, University of Abuja, Nigeria.

This article proposes a 'top-down' approach to developing glaucoma services. To do this, good evidence, gathered through research, is needed about the following:

- The prevalence of different types of glaucoma in the population (as open-angle and angle-closure glaucoma are managed differently).
- The age and socio-economic status of the local population, as well as any biomedical/metabolic or genetic factors that might predispose them to glaucoma. This makes it possible to identify the high-risk groups.
- The local community's knowledge, beliefs and health-seeking behaviour with regards to eye disease.
- The expectations and perceptions of patients and family members.
- The best treatment options (based on randomised controlled clinical trials and outcomes studies), which take into account the local realities and patients' preferences.

All of the above can be used to develop efficient, streamlined services that will encourage patients to come back for long-term care and follow-up, which is essential.

Suggested steps

The initial focus should be on developing good quality sub-speciality services at the tertiary level, followed by strengthening of secondary eye care (at district level) and then implementation of strategies for the early detection of glaucoma. There should be clear guidelines for referral (in both directions) between tertiary and secondary levels, and from the community to the secondary level once early detection strategies are implemented.

If this approach is ignored, early detection and diagnosis will create false expectations – and eventually disappointment – when patients are told nothing can be done about their diagnosis due to inadequate services at secondary or tertiary level. This will lead to a loss of faith in the eye care service.

The fives steps in this approach are described below.

Step 1. Strengthen tertiary eye care units to provide a good standard of glaucoma services

Mohammed Abdull

Glaucoma care requires skilled personnel who can work in teams

It must be possible for patients to undergo all the necessary investigations during a single visit. This will reduce costs to patients and encourage them to come back for follow-up visits. The following are also needed at tertiary level:

- **Equipment.** The hospital should be equipped with the appropriate diagnostic and therapeutic equipment.
- **Skilled personnel.** The glaucoma team should consist of glaucoma sub-specialists, general ophthalmologists, optometrists, ophthalmic nurses, counsellors, equipment technicians and other allied eye care providers. The team should be trained to provide accurate diagnosis and prompt, appropriate management with a choice of medical, laser or surgical treatment. Personnel should be able to monitor disease progression and institute treatment using clear clinical guidelines. Task sharing may be required, such as training nurses or technicians to assess visual fields, to take optic disc images or to counsel patients so that clinicians have time to focus on management decisions.
- **Information management.** There should be robust health management information systems and reliable management of medical records to ensure follow-up and monitoring of disease progression.

Step 2. Strengthen secondary centres (at district level) to manage less complex cases

- There should be a robust referral and feedback system between the tertiary centre and the secondary centres.
- Protocols for ocular examination and glaucoma diagnosis and management should be in place.
- Non-complex glaucoma cases should be managed at the secondary centres. Additionally, patients that had surgery or laser treatment at the tertiary centre can be referred back to the secondary centres for long-term care and follow-up.

Step 3. Develop glaucoma case-detection strategies at the secondary and primary levels

For example, everyone aged 30 (or 40) years and above who seeks eye care (e.g. with presbyopia or refractive errors) and for driving tests, could be offered a comprehensive eye examination, including optic disc assessment and intraocular pressure measurement, with confirmation of glaucoma diagnosis by visual field testing.

Step 4. Provide low vision and rehabilitation services

Glaucoma is the commonest cause of functional low vision in Nigeria.[1] Providing low vision services for glaucoma patients could therefore enhance their functional vision and quality of life.

If a high proportion of the glaucoma patients who come forward are already blind, community-based rehabilitation (CBR) should be an integral part of the glaucoma service provided.

Step 5. Increase awareness of glaucoma among policy makers and the public

Develop good working relationships with people responsible for health policy, whether at a local or national level. Emphasise that glaucoma is a major cause of irreversible blindness that could potentially be avoided. Encourage policy makers to create supportive policies: for example, to enhance the availability of affordable glaucoma medication and laser treatment at an affordable cost.

A public health awareness campaign for glaucoma should only be instituted when a good glaucoma service is in place. The campaign should be based on local beliefs, attitudes and behaviour, and should make use of suitable communication channels. For example:

- placing posters in public areas
- giving talks and handing out leaflets in hospital waiting rooms
- working with local organisations
- using the media (e.g. radio or television programmes and newspaper articles).

Reference

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Chapter 14

Improving services for glaucoma care:

Implications for policy and programmes to achieve Universal Health Coverage

A procession of unmounted horses symbolic of past kings; at a Borno Durbar – a show of loyalty and readiness to engage

A perspectives paper proposing ways to apply the evidence derived from this study for improving glaucoma care services

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Thesis Title	Evidence for improving services for glaucoma in Nigeria

If the Research Paper has previously been published please complete Section B, if not please move to Section C

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Please list the paper's authors in the intended authorship order:	F Kyari, CE Gilbert, K Blanchet, R Wormald
Stage of publication	Undergoing peer review

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Supervisor Signature: CGilbert **Date:** 20 December 2016

Title page

Category: Global issues

Title: Improving Services for Glaucoma Care in Nigeria: Implications for Policy and Programmes to Achieve Universal Health Coverage

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SUMMARY

Glaucoma in Africa is sometimes referred to as the silent thief of sight. In Nigeria, glaucoma is common, it is serious, ophthalmologists face many constraints in managing it, people do not even know they have it until it is advanced, patients do not understand or comply with treatment after they are diagnosed and the poor are more likely to be glaucoma blind. Available evidence indicates that the health system in Nigeria is failing to meet the needs of glaucoma patients. Based on evidence, we propose future directions for improving services for glaucoma care in Nigeria, and the implications for policy and programmes to control glaucoma blindness, using a health systems-oriented approach. Three complementary strategies are required: (i) strengthening clinical services for glaucoma – by developing models of glaucoma care, improving clinical treatment options, making medicines and equipment available, financing glaucoma care and training eye care workers; (ii) introducing initiatives for earlier detection of glaucoma in the clinic and approaches in the community; and (iii) strengthening health system governance.

Glaucoma is a complex disease to manage and addressing it as a public health problem is challenging. However, we need to change the paradigm to recognise that glaucoma is a potentially avoidable cause of blindness in Africa.

INTRODUCTION

The United Nations resolution on Universal Health Coverage (UHC) is fundamental to achieving Sustainable Development Goal no. 3 - equity in health for everyone. This entails not only improving access to quality health services but also protection against financial risks in accessing services.[1] In line with UHC, a Global Action Plan 2014-2019 was developed for eye care,[2] which aims to ensure that eye diseases that cause blindness and visual impairment are addressed through universal standards of eye care that address local priorities.

Glaucoma is a group of eye diseases characterised by progressive optic neuropathy with visual field loss which can lead to irreversible blindness. Glaucoma affected more than 64.3 million globally in 2013, and is projected to increase to 76 million by 2020.[3] Primary open angle glaucoma (POAG) is the most common type, affecting 57.5 million people in 2015, increasing to 65.5 million by 2020.[4]

Glaucoma in Africa is sometimes referred to as the *silent thief of sight*,[5] and available evidence indicates that the health system in Nigeria is failing to meet the needs of glaucoma patients. Based on our findings[6-10] (summarised in Figure 1), we propose future directions for improving services for glaucoma care in Nigeria, and the implications for policy and programmes to control glaucoma blindness, using a health systems-oriented approach. Some of our recommendations also derive from major meetings on glaucoma in Africa: The Africa Glaucoma Summit in Accra, Ghana (2010)[11] and the Public Health Control of Vision Loss from Glaucoma in Africa Workshop in Kampala, Uganda (2012)[12] as well as relevant publications.[13, 14] The strategy we recommend is to target those in greatest need for glaucoma care to prevent them from going blind, supported by policies and funding mechanisms for service delivery, and clinical and operational research. At the same time, there is a need for health partnerships and social policies to address poverty through improved education and literacy, entrepreneurship and wealth creation.

GLAUCOMA IN NIGERIA

Data from the 2009 Nigeria national blindness and visual impairment survey (thereafter referred to as the Nigeria Blindness Survey) indicated that 4.2% of adults aged 40 years and above were blind.[15] Glaucoma was the second commonest cause of blindness (16.7%),[16] principally open angle glaucoma (OAG) (86% of all glaucoma).[6] In 2009, 5% of survey participants had glaucoma, affecting an estimated 1.8 million adults, and one in five were blind i.e. had a presenting visual acuity (VA) of less than 3/60 in the better eye. Ninety-four per cent were not diagnosed and not receiving care.[6] Independent risk factors for OAG were higher intraocular pressure (IOP), increasing age and Igbo ethnicity.[7] People of low socio-economic status were approximately four times more likely to be blind from glaucoma,[8] reflecting limited awareness of glaucoma and poor access to care. Additionally, ophthalmologists face many constraints in managing it.[9]

From the Nigeria Blindness Survey, it is estimated that per million population, 10,500 adults (aged 40 years and above) have glaucoma. The following definitions were used to estimate the number affected by level of severity, using the most affected eye: severe/advanced glaucoma – VA<3/60, vertical cup:disc ratio (VCDR) >0.8 and central visual field (CVF) of <10^o; moderate glaucoma – any level of VA with VCDR>0.7 and CVF of 10-20^o; early/mild glaucoma – any glaucomatous visual field defect and VCDR ≥0.7. Blind/end-stage glaucoma was defined as VA<3/60 in the better eye with a VCDR of 1.0.[17] There are estimated to be 5,900 (56%) adults per million population with severe/advanced disease, often blind in one eye and/or with severe visual impairment in the other eye, 2,100 (20%) moderate cases, 400 (4%) early cases and a further 2,100 (20%) are blind in both eyes.

Several factors contribute to the high prevalence of glaucoma blindness in Nigeria. These include low rates of early detection and diagnosis,[17] lack of specialist equipment and treatment options, lack of specialist glaucoma clinics and care pathways, poor compliance with treatment and follow-up,[9] the high cost of accessing care and treatment costs,[18] and lack of awareness and public knowledge about glaucoma compounded by socioeconomic deprivation.[10] The number of eye health workers in Nigeria, including ophthalmologists and optometrists, falls short of World Health Organization recommendations.[19, 20] In addition, Nigeria does not have an eye health policy and the national strategic plan for eye care is not uniformly implemented.

Considering these factors, three complementary strategies need to be put in place to reduce glaucoma blindness: (i) strengthening clinical services for glaucoma; (ii) introducing initiatives for earlier detection of glaucoma; and (iii) strengthening health system governance.

STRENGTHENING CLINICAL SERVICES FOR GLAUCOMA

Developing models of glaucoma care

There are currently no published articles on models of glaucoma care in Africa. A conceptual framework and systems approach for improving services for glaucoma in Nigeria are shown in Figure 1. Clinical, operational and health system research need to be embedded in care delivery models to determine optimal ways to improve access and acceptance of cost-effective treatment, to improve patients' hospital experiences and compliance rates, to promote follow-up of patients with stable disease in district eye departments, and for the earlier detection of glaucoma in the community.

Improving clinical treatment options

The treatment recommended for glaucoma in Africa depends on several factors. Medical therapy is often the first-line of treatment, with β-blockers being the most commonly used in Nigeria. Prostaglandin analogues (PGAs) are effective in preventing progression of visual field loss in the United Kingdom population,[21] but their use in Nigeria is limited due to their high cost. Other constraints include poor compliance with medicines and uncertain potency of topical preparations, which are usually kept in high ambient temperatures. One-off interventions are recommended in Africa, one being primary trabeculectomy with antimetabolites or β-irradiation, with a suggested 'glaucoma surgical rate' of 800 glaucoma surgeries per million population per year.[22] Indeed, skilful trabeculectomy with a joint care plan and adequate follow-up may be a good option but acceptance of surgery can be very low.[9, 17] Laser therapy seems a safe and acceptable alternative, which reduces costs to patients, as an inpatient stay is not required. Although the initial capital outlay for lasers is high, they can be used to treat other eye conditions, and can function for many years. An effective, safe, affordable and acceptable one-off treatment is the first essential building block of glaucoma care in Africa, particularly for the poor and illiterate and those who live far from eye care facilities. Treatment modalities need to be assessed in randomised controlled trials (RCTs) to determine the most cost-effective and acceptable treatment for patients and providers in the African context.

Making medicines, surgery and laser treatment available

To improve access to treatment, institutions need to be strengthened with equipment and training in surgical skills and laser procedures, with the development of glaucoma care teams. Tertiary institutions should have specialist glaucoma clinics which are adequately resourced so that a full assessment and definitive diagnosis can be made at the first visit, with counselling of patients and their carers about treatment and the need for long-term follow-up.

Relevant government ministries/agencies are urged to improve the supply chain of glaucoma medications and surgical consumables through tax and import duty waivers, and by providing an enabling environment for local production of glaucoma medication. Pharmaceutical companies could be called upon to provide PGAs free of charge to the poorest, and global technology partners should make lasers and accessories (lenses, probes, protective goggles, etc.) more affordable for service providers in low/middle income countries.

Financing glaucoma care

No patient should receive suboptimal care because they cannot afford treatment. Strategies for healthcare financing for glaucoma to contain costs need to be developed and evaluated. One approach could be to provide free treatment to poor patients. Another is to advocate that more potent medications such as PGAs, and trabeculectomy and laser procedures be covered by health insurance. UHC through government budgetary allocations is probably the most sustainable approach for such a chronic, serious and life-long disease.

Human resources for eye health

In order to improve services for glaucoma, multi-tasking by health workers is recommended with, for example, nurses being trained to perform optic nerve head photography and visual field analysis. Early detection of significant glaucoma through community-based opportunistic case-detection by optometrists, follow-up in the community and community-based care especially for post-operative cases by ophthalmic nurses, and testing for vision loss by primary healthcare workers are also strategies to explore. Agreement on professional boundaries will be required, with clearly defined work areas for allied eye care members of the glaucoma care team, and clearly defined roles for glaucoma care in secondary centres.[23]

Health information system

Health management information systems are essential for improving glaucoma services in Nigeria to provide good medical records systems to track patients over time and monitor trends of treatment. We recommend that the number of procedures for glaucoma, as well as the number of cataract operations, be monitored and reported centrally. Good medical records are also important for robust referral/feedback systems, to document clinical findings for follow-up and to develop a database of glaucoma patients.

APPROACHES FOR EARLIER DETECTION OF GLAUCOMA

Before starting any intervention for case-detection, adequate clinical services for glaucoma must be in place. The challenge of a public health glaucoma care programme would be to find people who already have significant glaucoma and ensure they have access to services to reduce the risk of progression to bilateral blindness. The poorest in the population need to be targeted because glaucoma blindness affects them the most.

In the clinic

Primary eye care, including that provided by optometrists who are few in number and usually located in urban areas, is almost entirely lacking in Nigeria, as in many countries in Africa, and so there are no mechanisms for early detection of glaucoma. One solution to improve earlier detection of glaucoma is to ensure that all adults aged 40 years and above who present to eye care services, regardless of their presenting complaint, undergo routine optic disc assessment. This approach was effective in the eye department in Bauchi, North-eastern Nigeria, where the optometrists referred anyone with a CDR ≥0.6 to the ophthalmologist for examination.[17]

Identified high-risk groups and first-degree relatives (FDRs) of patients with glaucoma should also be targeted.

Community approaches

We advocate that optic disc assessment of all those aged 40 years and above become an integral component of outreach eye care activities with a referral of those with VCDR$\geq$0.6 to designated facilities for full assessment, definitive diagnosis and treatment. Another assessment to consider at the community level is a properly conducted swinging flashlight test to detect relative afferent pupillary defects (RAPD) which has to the potential to find at least 25% of glaucoma,[24] and with strong specificity for glaucoma.[25]

Figure 2 shows a possible algorithm for glaucoma case-detection at community and clinic levels. In a retrospective evaluation of outreach in Ibadan, people referred from outreach were twice as likely to have mild/moderate glaucoma than patients referred from other facilities who had more severe disease.[26]

Another strategy is to integrate optic disc imaging using mobile phone apps into screening activities for non-communicable diseases, or into programmes for the control of onchocerciasis (river blindness) and trachoma, which are reaching a high proportion of the most vulnerable population in Nigeria.

Informal providers of healthcare, who are ubiquitous and acceptable to community members in Africa, could also be engaged in identifying individuals suspected of having glaucoma. For example, in Nassarawa, spectacle vendors were enrolled in a study to assess interventions for finding cases of glaucoma in the community. About half of those referred by spectacle vendors subsequently attended the eye clinic, 15% of whom were newly diagnosed with glaucoma. (Personal communication: HI, MSc PHEC dissertation, LSHTM 2016).

Other approaches for earlier detection may include designing and implementing a community awareness strategy, using local terms such as those in Hausa that describe behaviour associated with peripheral visual field loss (e.g. *taka shanya*), through social and mass media platforms such as radio which has a wide reach, television, and newspapers. For example, people could be encouraged to regularly check the vision of each eye by covering the other eye. Community awareness strategies should be planned carefully to avoid creating a demand that cannot be met. However, greater demand is needed to generate political pressure that may drive the development of better services.

STRENGTHENING HEALTH SYSTEMS GOVERNANCE

A strong health system requires leadership and governance to deliver improved care, based on evidence of what works, as day-to-day monitoring and interval evaluation can improve services. Additionally, it is important that team leaders take part in developing policies to include glaucoma in national healthcare plans and to integrate eye care into programmes for non-communicable diseases. Data and information are also required for advocacy with policy makers and for the engagement of civil society to improve health education, knowledge and public awareness.

Glaucoma patients' associations can be strengthened to support vulnerable groups through sharing experiences and resources by patients and family advocates.

CONCLUSION

Glaucoma is a complex disease to manage and addressing it as a public health problem is a challenge. However, we need to change the paradigm to recognise that glaucoma is a potentially avoidable cause of blindness in Africa. We have discussed possible ways in which to improve services for glaucoma in Nigeria with the aim of ensuring inclusion of those most at risk of blindness from glaucoma i.e. the poor. Further clinical and operational research is required to address the acknowledged evidence gaps. We also advocate for policies to make glaucoma treatment available and affordable to all, and possibly free to the poor.

Rather than remaining silent, let us give glaucoma patients a voice so that the silent thief of sight does not lead them into darkness.

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Competing interests

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Contributorship statement

FK led the conception and design of the study and drafted the manuscript and edited it with consideration of input from co-authors. CG supervised the conception and design of the study and revised the article for important intellectual content.

KB and RW contributed to the design of the study and revised the article for important intellectual content.

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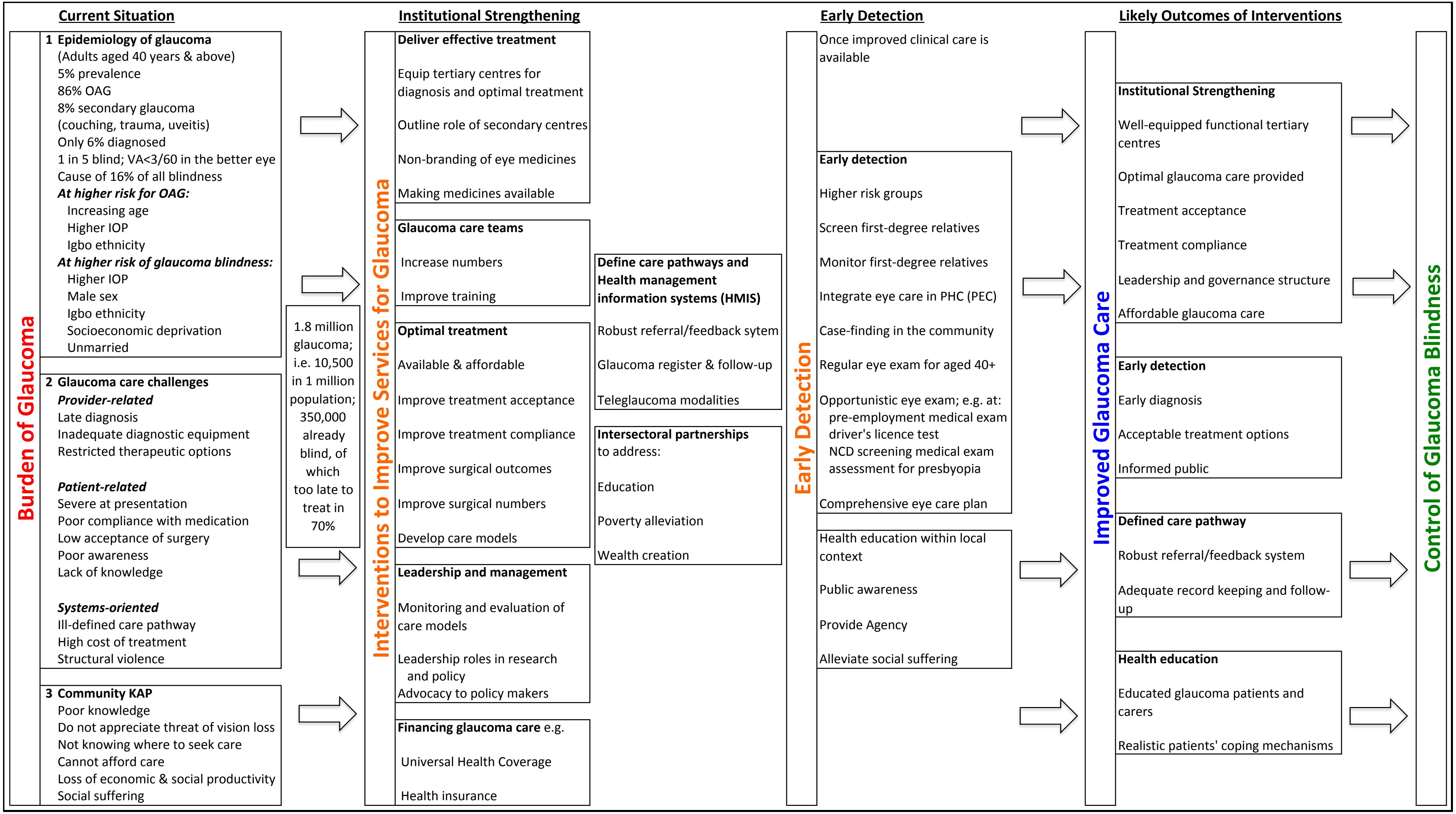
FIGURES

Figure 1. Conceptual framework for improving services for glaucoma in Nigeria

Figure 2. Algorithm for glaucoma case-detection at community and clinic levels by assessment of cup:disc ratio and relative afferent pupillary defect

Figure 1. Conceptual framework for improving services for glaucoma in Nigeria



Current Situation

Burden of Glaucoma

1 Epidemiology of glaucoma
(Adults aged 40 years & above)
5% prevalence
86% OAG
8% secondary glaucoma
(couching, trauma, uveitis)
Only 6% diagnosed
1 in 5 blind; VA<3/60 in the better eye
Cause of 16% of all blindness
At higher risk for OAG:
Increasing age
Higher IOP
Igbo ethnicity
At higher risk of glaucoma blindness:
Higher IOP
Male sex
Igbo ethnicity
Socioeconomic deprivation
Unmarried

2 Glaucoma care challenges
Provider-related
Late diagnosis
Inadequate diagnostic equipment
Restricted therapeutic options

Patient-related
Severe at presentation
Poor compliance with medication
Low acceptance of surgery
Poor awareness
Lack of knowledge

Systems-oriented
Ill-defined care pathway
High cost of treatment
Structural violence

3 Community KAP
Poor knowledge
Do not appreciate threat of vision loss
Not knowing where to seek care
Cannot afford care
Loss of economic & social productivity
Social suffering

1.8 million glaucoma; i.e. 10,500 in 1 million population; 350,000 already blind, of which too late to treat in 70%

Institutional Strengthening

Interventions to Improve Services for Glaucoma

Deliver effective treatment

Equip tertiary centres for diagnosis and optimal treatment

Outline role of secondary centres

Non-branding of eye medicines

Making medicines available

Glaucoma care teams

Increase numbers

Improve training

Optimal treatment

Available & affordable

Improve treatment acceptance

Improve treatment compliance

Improve surgical outcomes

Improve surgical numbers

Develop care models

Leadership and management

Monitoring and evaluation of care models

Leadership roles in research and policy
Advocacy to policy makers

Financing glaucoma care e.g.

Universal Health Coverage

Health insurance

Define care pathways and Health management information systems (HMIS)

Robust referral/feedback sytem

Glaucoma register & follow-up

Teleglaucoma modalities

Intersectoral partnerships to address:

Education

Poverty alleviation

Wealth creation

Early Detection

Early Detection

Once improved clinical care is available

Early detection

Higher risk groups

Screen first-degree relatives

Monitor first-degree relatives

Integrate eye care in PHC (PEC)

Case-finding in the community

Regular eye exam for aged 40+

Opportunistic eye exam; e.g. at:
pre-employment medical exam
driver's licence test
NCD screening medical exam
assessment for presbyopia

Comprehensive eye care plan

Health education within local context

Public awareness

Provide Agency

Alleviate social suffering

Likely Outcomes of Interventions

Improved Glaucoma Care

Institutional Strengthening

Well-equipped functional tertiary centres

Optimal glaucoma care provided

Treatment acceptance

Treatment compliance

Leadership and governance structure

Affordable glaucoma care

Early detection

Early diagnosis

Acceptable treatment options

Informed public

Defined care pathway

Robust referral/feedback system

Adequate record keeping and follow-up

Health education

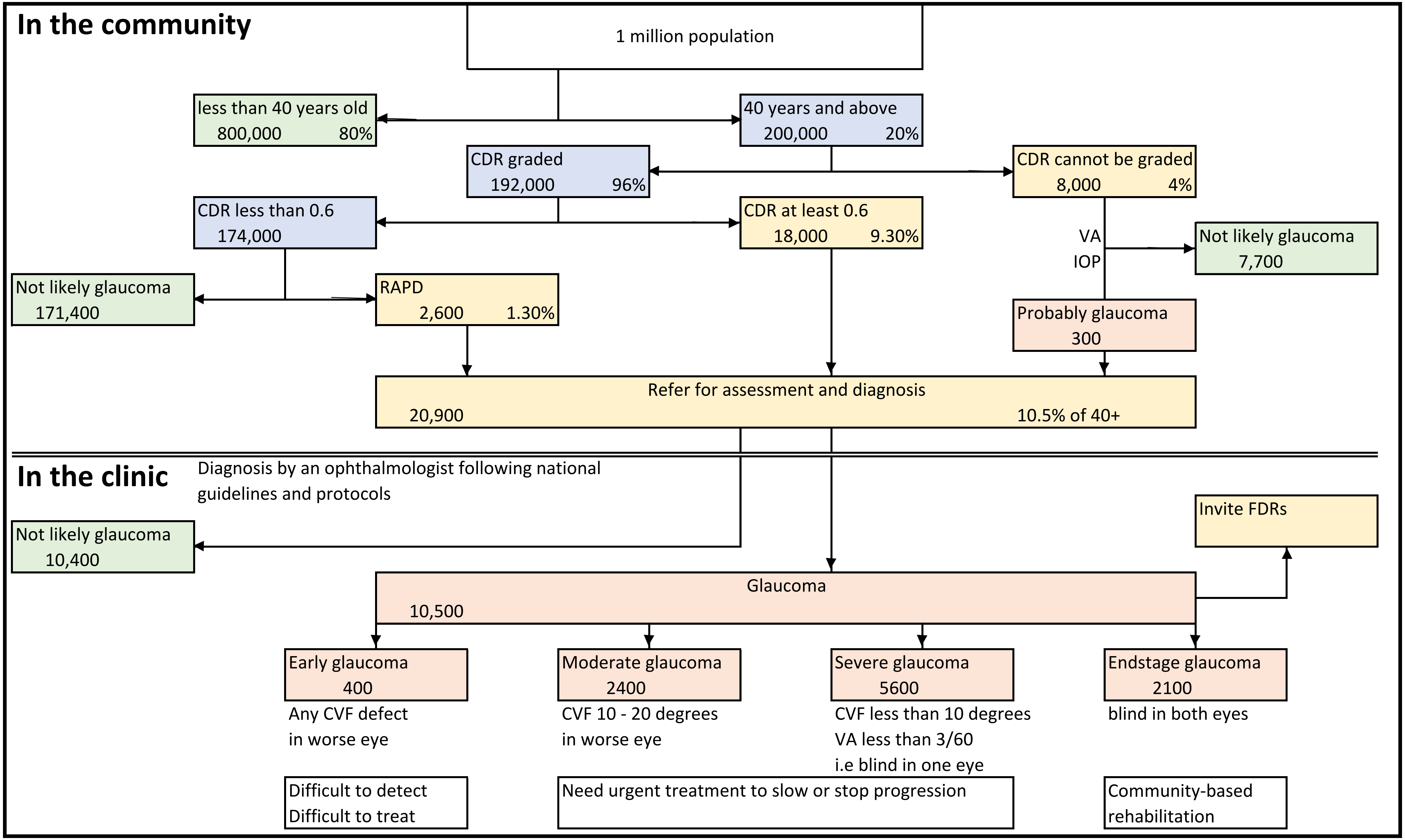
Educated glaucoma patients and carers

Realistic patients' coping mechanisms

Control of Glaucoma Blindness

OAG = open-angle glaucoma; VA = visual acuity; IOP = intraocular pressure; KAP = knowledge, attitude & practice; PHC = primary health care; PEC = primary eye care; NCD = non-communicable diseases.

Figure 2. Algorithm for glaucoma case-detection at community and clinic levels by assessment of cup:disc ratio and relative afferent pupillary defect



CDR - cup:disc ratio; VA - visual acuity; IOP - intraocular pressure; RAPD - relative afferent pupillary defect; FDRs - first degree relatives; CVF - central visual fields.
Numbers do not show glaucoma in persons younger than 40 years

Chapter 15

Implications for research

Adun Ogunro

Diode laser micropulse trabeculoplasty

Implications for research and future work drawn from all the contributing work

Implications for research

Glaucoma is a major public health problem and a leading blinding eye disease in Africa; and up to 90% remains undiagnosed.[1] The aim of this work was to determine ways in which to improve service delivery for glaucoma care in Nigeria in order to control glaucoma blindness. The study demonstrated a high prevalence of glaucoma, a high proportion of glaucoma blindness and many challenges for glaucoma care in Nigeria. The findings imply the need for public health control strategies with high quality integrated glaucoma care services to improve quality of life, and reduce morbidity and blindness.

Define treatment modality

There is a need to provide evidence-based optimal clinical care; and our top priority for research is to define appropriate choice of a one-off treatment modality that is effective, acceptable, affordable and sustainable. This can be determined by multi-centre randomised controlled trials (RCTs) comparing treatment outcomes and economic advantages of intraocular pressure (IOP) lowering therapies. For example, a study of topical medication versus selective laser trabeculoplasty (SLT) or diode laser micropulse trabeculoplasty (DLT), trabeculectomy with antimetabolites versus laser therapy, transcleral diode laser cyclophotocoagulation versus trabeculectomy, etc. There are currently no such RCTs being undertaken in Nigeria. Initial results of transcleral diode laser cyclophotocoagulation in refractory glaucoma showed unsustained lowering of IOP.[2] However, more recently, the results of a prospective monitoring of transcleral diode laser cyclophotocoagulation in seeing glaucoma eyes are being analysed and the therapy seems promising.[3] If the results are acceptable, then ways to make the treatment scalable will be the next step. Although the diode laser machine has an initial high capital outlay, it is versatile and can be used for many other treatments and it can be used repeatedly for a long time. Prospective monitoring of outcomes of trabeculectomy with 5-flourouracil has shown significant benefits in lowering IOP beyond three months[4] and complete success with IOP<21mmHg at one year.[5] However, there have been no studies comparing different surgical methods or adjunctive therapy.

Acceptance of surgical treatment and continuation of medical treatment is usually low. Motivational interviewing for glaucoma (MIG) was designed to strengthen patients' personal motivation and their exploration of reasons for change in an atmosphere of understanding, acceptance and compassion. An RCT for MIG compared with standard care and regular glaucoma information to patients is being undertaken to assess whether MIG will increase the uptake of treatment.[6] This approach is potentially scalable and may be included in improved glaucoma care guidelines to enhance treatment acceptability.

Clinical guidelines and protocols of management

Clinical care may also be improved if we develop an algorithm for choice of therapy and continued management using weighted scores for patient, facility and community characteristics; taking into account local realities and informed patients' preferences. For example, a young patient with moderate glaucoma may be advised to have trabeculectomy with adjunctive antimetabolite; or an elderly man with access to a glaucoma clinic may be treated with topical latanoprost. With appropriate choice of therapy, clinical guidelines and protocols of management can then be defined and care teams developed to provide optimal glaucoma management. These steps may be undertaken by the Nigerian Glaucoma Society within the context of operational research and involving monitoring of outcomes tools. Additionally, another implication is an evaluation research to assess whether use of clinical guidelines and protocols improve practice patterns.

Determine approaches to earlier detection of cases

The second priority for research is to determine approaches to earlier detection of glaucoma cases. This will involve case-detection of patients in healthcare facilities and approaches to case-finding in the community with a clear care pathway.

The envisaged outcome of these research priorities is institutional strengthening for high quality optimal glaucoma service in the hospitals with 2-way referral/feedback systems.

In this regard, we are in the process of developing online forums for discussion on “tertiary institutional strengthening for high quality optimal glaucoma care in Africa” and on “glaucoma treatment” on the platform of the World Glaucoma Association Africa project, which I will lead. This strategy is the first step in our glaucoma care development ladder. I am part of the team that developed the International Agency for the Prevention of Blindness (IAPB) essential list of equipment for glaucoma, which will be launched at the IAPB 10th general assembly (10GA) in October 2016. I am also a convener of a glaucoma course at the 10GA. This course will describe the challenges and solutions of glaucoma care in Africa. Challenges from the patients’ perspectives as well as from the service provider perspectives will be discussed. On-going glaucoma sub-specialty training initiatives and intervention trials will be presented, with opportunities for discussion. The development of a model of high-quality glaucoma service in sub- Saharan Africa will be described. This includes programme planning and implementation, clinical care and public health interventions for the control of glaucoma blindness. Recommendations at the last ‘Glaucoma in Africa’ meeting in Kampala[7] will be discussed with a focus on targets achieved and determining next priorities and strategies.

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List of Appendices

Appendix 1a

LONDON SCHOOL OF HYGIENE
& TROPICAL MEDICINE

ETHICS COMMITTEE

APPROVAL FORM

Application number: **5657**

Name of Principal Investigator	**Clare Gilbert**
Department	**Infectious and Tropical Diseases**
Head of Department	**Professor Simon Croft**

Title: **Glaucoma in Nigeria: prevalence, types and risk factors for glaucoma and glaucoma blindness, situational analysis of physicians' management practice pattern, and patients and community perception of the disease**

This application is approved by the Committee.

Chair of the Ethics Committee .... T. W. Meade ....

Date 25 February 2010

Approval is dependent on local ethical approval having been received.

Any subsequent changes to the application must be submitted to the Committee via an E2 amendment form.

Appendix 1b

National Health Research Ethics Committee of Nigeria (NHREC)
Promoting Highest Ethical and Scientific Standards
for Health Research in Nigeria

Federal Ministry of Health

Protocol Approval Number: NHREC/01/01/2007-14/04/2010
NHREC Protocol Number: NHREC/01/01/2007-09-02-2010

Date: April 14, 2010

Re: Glaucoma in Nigeria: prevalence, types and risk factors for glaucoma and glaucoma blindness; situational analysis of physicians' management practice pattern; and patients' and community perception of the disease

Health Research Ethics Committee assigned number: NHREC/01/01/2007
Name of Principal Investigator: Dr. Claire Gilbert

Address of Principal Investigator: Professor in International Health and
Co-Director International Centre for Eye Health (ICEH)
LSHTM

Date of receipt of valid application: 09-02-2010
Date of meeting when final determination of research was made: 14-04-2010

Notice of Full Approval after full Committee Review

This is to inform you that the research described in the submitted protocol, the consent forms, advertisements and other participant information materials have been reviewed and *given full approval by the Health Research Ethics Committee.*

.

This approval dates from 14/04/2010 to 13/04/2011. If there is delay in starting the research, please inform the HREC so that the dates of approval can be adjusted accordingly. Note that no participant accrual or activity related to this research may be conducted outside of these dates.

All informed consent forms used in this study must carry HREC assigned protocol approval number and duration of HREC approval of the study. In multiyear research, endeavor to submit your annual report to the HREC early in order to obtain renewal of your approval and avoid disruption of your research.

The National Code for Health Research Ethics requires you to comply with all institutional guidelines, rules and regulations and with the tenets of the Code including ensuring that all adverse events are reported promptly to the HREC. No changes are permitted in the research without prior approval by the HREC except in circumstances outlined in the Code. The HREC reserves the right to conduct compliance visit to your research site without previous notification.

For: Clement Adebamowo BMChB Hons (Jos), FWACS, FACS, DSc (Harvard)
Chairman, National Health Research Ethics Committee of Nigeria (NHREC)

Department of Health Planning, Research & Statistics
Federal Ministry of Health
11th Floor, Federal Secretariat Complex Phase III
Ahmadu Bello Way, Abuja

Tel: +234-09-523-8367
E-mail: chairman@nhrec.net, secretary@nhrec.net,
deskofficer@nhrec.net,
URL: http://www.nhrec.net,

Fatima Kyari - Re: Resending: Updating ethics approval for my PhD: Glaucoma in Nigeria NHREC 01/01/2007

From: aminu yakubu <yaminads@yahoo.com>
To: Fatima Kyari <Fatima.Kyari@lshtm.ac.uk>
Date: 06/03/2015 00:17
Subject: Re: Resending: Updating ethics approval for my PhD: Glaucoma in Nigeria NHREC 01/01/2007
Cc: Aminu Yakubu <deskofficer@nhrec.net>

My dear sister,

Greetings. I am writing further to your mails. I am to inform you that once contact with primary data sources are completed, we do not require that researchers maintain a subsisting ethics approval for data analysis and report writing phases. You may therefore wish to proceed with your writing and dissemination please.

All the best.

Aminu A. Yakubu
NHREC Administrative Officer
Department of Health Planning and Research,
Federal Ministry of Health
PMB 083, Abuja
+234 80 6547 9926
yaminads@yahoo.com
http://nhrec.net

On Friday, 12 December 2014, 17:47, Fatima Kyari <Fatima.Kyari@lshtm.ac.uk> wrote:

Dear Aminu,

Thank you very much for the response and instruction.

Please find attached the letter of request and the progress report, which I hope will support my request.
Please let me know if you need further information.

Warm regards
Fatima

>>> Aminu Yakubu <yaminads@yahoo.com> 30/11/2014 08:44 >>>
Dear Dr. Kyari,

Greetings and apologies for this late response. Please submit a progress report with a forwarding letter seeking continuing review approval.

Regards Ma.

On Nov 13, 2014, at 3:48 PM, Fatima Kyari <fatima.kyari@lshtm.ac.uk> wrote:

>>> Fatima Kyari 13/11/2014 14:46 >>>

Dear Aminu,

I would like to update the ethics approval for my PhD research at the London School of Hygiene and Tropical Medicine. All fieldwork is completed and I am at the writing up and dissemination stage.

Please could you kindly advise on the next step.

Thank you

Fatima

Appendix 2

Nigeria National Blindness and Low Vision Survey

Demographic Information

Subject Serial Number ☐☐☐ Household Serial Number ☐☐☐ Personal Identification Number (PIN) ☐☐☐ Study Code ☐☐☐☐☐☐☐☐☐☐

☐☐	☐☐						
Day	Month	Geo-political Zone	State	LGA	Village / Town	Street Block	Rural / Urban

Name ___________________________ Marital status 1=Single 3=Widowed 2=Married 4=Separated/Divorced ☐ Sex 1=Female 2=Male ☐ Age (years) ☐☐ **Special Case (1:7 =40)** 1=Yes, 2=No ☐ Ethnic group ________________

What kind of work, if any, do you mainly do? 1) ____________________________________
2) ____________________________________

If you work in agriculture, do you work on: 1 = Your own land or your family's land 2 = Rented land 3 = Someone else's land 9=No agriculture work ☐

What is your religion? 1 = Islam 2 = Christianity 3 = Other ________________ ☐

Have you ever attended school? 1=Yes 2=No ☐ Highest level of school attended? 1=Primary (1-6) 2= Jr Secondary (7-8) 3= Sr Secondary (9-11) 4=University/Polytechnic 5= Koranic school ☐ Highest class / grade completed at that level? ☐ Are you able to read or write? 1=Easily 2=With difficulty 3=Not at all ☐

Age at start of school 99= Never went to school ☐☐ Age at leaving school ☐☐ Main language _________ Other languages __________ __________ Water 1 =House tap 3 = House well 2 = Street tap 4 = Village Well 5 = Surface water (stream, lake) ☐

Latrine 1 = Flush toilet 2 = Pit latrine 3 = Bush ☐ BP: Systolic / Diastolic 888=Refused, 999=Machine failed/Not available ☐☐☐ / ☐☐☐ *(BP to be taken in adults only)* Height ☐☐☐.☐ Wt(Kg) ☐☐☐.☐

Presenting Visual Acuity (D = distance glasses)

Has no D-Glasses ☐ Arrives with D-Glasses ☐ Forgot D-Glasses ☐ Given Glasses But not using ☐

At what age did you start wearing glasses? (99 = Never has worn glasses) ☐☐

Wears glasses for reading? 1 = Yes 2=No ☐

Vision WITHOUT glasses	**R**	**L**
Number letters seen at 4m:	☐☐	☐☐
Misses at least 1 E on top line at 4m, move to 1m.		
Number letters seen at 1m:	☐☐	☐☐

Cannot see at 1m (Note: To be completed by Ophthalmologist)

(Please tick correct box)	**R**	**L**
Counting fingers (at 1m):	☐	☐
Hand movements:	☐	☐
Perception of light:	☐	☐
No perception light (test in dark):	☐	☐

Cannot be tested

R	**L**
☐	☐

1= Believed blind

2= Believed not blind

If RED CARD, test both eyes without wearing glasses at 4m and / or 1m, as needed. Remember to change the version of the 'E' chart.

4m ☐☐

1m ☐☐

If wearing habitual distance spectacles, repeat VA WEARING GLASSES:

	R	**L**	**BE**
Number letters seen at 4m:	☐☐	☐☐	☐☐
Misses at least 1 E on top line at 4m, move to 1m.			
	R	**L**	**BE**
Number letters seen at 1m:	☐☐	☐☐	☐☐

GREEN CARD / RED CARD

Green / Red card G = Green, R = Red ☐ **YELLOW** ☐

Interviewer will mark specials (1:7 = 40 years) with YELLOW tag

Note: Red card for those 24 letters or less in one or both eyes

EXAMINERS INTIALS

Refraction (staple printout on sheet)

Right Eye:

Average Refractive Error and Keratometry:

mm

Sphere ± ☐ ☐☐.☐☐ R1 ☐☐.☐☐

Cylinder ± ☐ ☐☐.☐☐ R2 ☐☐.☐☐

Axis ☐☐☐

Deg R1 ☐☐☐

Auto / Manual ☐

R2 ☐☐☐

1=A 2=M 9=Subject did not understand **Av K (mm)** ☐☐.☐☐

(Record as 999 if no result)

Left Eye:

Average Refractive Error & Keratometry: **mm**

Sphere ± ☐ ☐☐.☐☐ **R1** ☐☐.☐☐

Cylinder ± ☐ ☐☐.☐☐ **R2** ☐☐.☐☐

Axis ☐☐☐

Deg R1 ☐☐☐

Auto / Manual ☐

R2 ☐☐☐

1=A 2=M 9=Subject did not understand **Av K (mm)** ☐☐.☐☐

(Record as 999 if no result)

For Red Cards

If no automated refraction result obtainable and subject is a **Red Card**: do objective refraction and write result above.

	R	L
Was manual refraction impossible? 1 = Yes, 2 = No	☐	☐

Best Corrected Visual Acuity (Wearing the refraction result)

For Red Card & Special ONLY	R	L	BE
Number letters seen at 4m:	☐☐	☐☐	☐☐
If misses at least 1 E on top line at 4m, move 1m:			
Number letters seen at 1m:	☐☐	☐☐	☐☐

Visual field analysis 1= Yes 2= No	**R**	**L**
Screening test for all=40 years only	☐	☐
Threshold test, if clinically indicated		

Ultrasound only if = 40 years

Right Eye: **1 = Successful, 2 = Not possible, 3 = Not understand** ☐

Axial Length: ☐☐.☐☐

ACD: ☐.☐☐

Lens: ☐.☐☐ **(Record as 999 if no result)**

Left Eye: **1 = Successful, 2 = Not possible 3 = Not understand** ☐

Axial Length: ☐☐.☐☐

ACD: ☐.☐☐

Lens: ☐.☐☐ **(Record as 999 if no result)**

EXAMINERS INTIALS

Previous Eye History and Examination for ALL subjects

History of 1) diabetes ☐ 2) hypertension ☐ 1 = Yes 2= No

3) glaucoma ☐ **4)** trachoma ☐

Clinical evidence of trachoma R L

TT 1 = Yes 2 = No 9 = no view ☐ ☐

CO 1 = Yes 2 = No 9 = no view ☐ ☐

None – now do not need this

Comment ______________________________

History of onchocerciasis 1 = Yes 2 = No ☐

Evidence of Onchocerciasis (Photo clue test) 1 = Yes 2 = No ☐

Ivermectin in last 12 months?
1 = Yes 2 = No 3= Does not apply - non-oncho area ☐

History of eye injury 1 = Yes 2 = No ☐

Cataract Grade (Mehra - Minassian): R ☐☐ L ☐☐
(0, 1, 2A, 2B, 3, 4, 5)

Evidence of surgery:

Eyelid: 1A = Yes (Trachoma) 1B = Yes (Other) 2 = No ☐ ☐

Cataract: 1 = Yes 2 = No ☐ ☐

Other surgery: 1 = Yes 2 = No ☐ ☐

Give details if 'Other surgery' : ______________________________

Cataract surgery only R L

Time (in months) since cataract surgery / couching: ☐☐ ☐☐

Location: ☐ ☐
1 = Hospital 2 = Eye Camp 3 = Home 4 = Other

Actual name of the place of operation (city/town / village) and location, e.g. Kaduna NEC

R______________________________

L ______________________________

Technique: 1 = ICCE, 2 = ECCE, 3 = Couching, 4 = Phaco ☐ ☐

IOL position : 1 = A/C IOL, 2 =P/C IOL, 3 = None ☐ ☐

Using aphakic spectacles: 1 = Yes 2 = No ☐ ☐

Pterygium R L

1A = Yes (visual axis) 1B = Yes (off axis) 2 = No ☐☐ ☐☐

Other **Conjunctival disease** 1 = Yes, 2 = No ☐ ☐

Details: ______________________________

Other **Corneal disease/scar** 1 = Yes, 2 = No ☐ ☐

Details: ______________________________

Anterior chamber / Iris disease ☐ ☐

1 = Yes, 2 = No, 3 = No view

(**Note: Specify if onchocerciasis is queried.)**

Details: ______________________________

Green Cards Only: Eye Examination

Un-dilated Optic Disc Cup / Disc Ratio (CDR):

R L

CDR 99 cannot assess ☐.☐ ☐.☐

CDR asymmetry = 0.2 1 = Yes 2 =No 9 = Cannot assess ☐

Optic disc haemorrhage? 1 = Yes 2 = No 9 = Cannot assess ☐ ☐

(Undilated, direct ophthalmoscopy)

R L

Vascular Retinopathy: 1 = Yes 2 = No 9 = Cannot assess ☐ ☐

Retinitis Pigmentosa: 1 = Yes 2 = No 9 = Cannot assess ☐ ☐

ARMD: 1 = Yes 2 = No 9 = Cannot assess ☐ ☐

Other disease: 1 = Yes 2 = No 9 = Cannot assess ☐ ☐
(Details)______________________________

Comment: ______________________________

Red cards:
Green cards with abnormal disc findings:
Yellows (Specials) for normative database
CONTINUE WITH FULL EXAMINATION.

EXAMINERS INTIALS

FULL EXAMINATION

Reason for full examination: (tick correct box/es)

1 = Red card ☐
2 = Special (1:7=40 years) ☐
3 = Green card with detected abnormality ☐
4 = Persons with known visual / eye problems ☐

(Extensive examination as clinically indicated) **R** **L**

Iris Colour 1=Brown, 2=Hazel, 2=Blue, 3=Green, 9 = Not seen ☐ ☐

Van Herick's **Grade** 0 - 4, 9 = Not possible ☐ ☐

Applanation IOP 99 = Not possible ☐☐ ☐☐

Gonioscopy 1 = Open, 2 = Closed, 9 = Not possible ☐ ☐

(Indications for gonioscopy: IOP = 20 mmHg; CDR > 0.6; CDR difference > 0.2; Van Herick's grades 0, 1, 2)

RAPD 1 = Yes, 2 = No, 9 = Not possible ☐

*** DILATE***

WHO grading: **R** **L**

Nuclear(0-3) or 7 = Aphakia; 8 = IOL; 9 = Cannot grade ☐ ☐
Cortical (0-3 +/- CEN) or 7 = Aphakia; 8 = IOL; 9 = Cannot grade ☐ ☐
PSCLO (0-3) or 7 = Aphakia; 8 = IOL; 9 = Cannot grade ☐ ☐
Hypermature 1 = Yes, 2 = No; 7 = Aphakia; 8 = IOL; 9 = Cannot grade ☐ ☐

Posterior capsular opacification (PCO) with IOL(s)
1 = YesPCO, 2 = Clear capsule, 3 = Not sure, 9 = Not applicable ☐ ☐

Disc Pathology 1 = Yes, 2 = No, 9 = No view ☐ ☐
Excluding myopia, large CDR, PPA.

Details:____

R **L**

Quality of view: 1= Good 2 = Poor 3 = None ☐ ☐
CDR ☐.☐ ☐.☐
CDR asymmetry (RCDR - LCDR) ☐
Abnormal is >0.2 1 = Abnormal, 2 = Not
Notch 1 = Yes, 2 = No ☐ ☐
Disc Haemorrhage 1 = Yes, 2 = No ☐ ☐

Diabetic retinopathy 1 = Yes 2 = No 9 = Not seen **R** **L**

Non-proliferative ☐ ☐
Proliferative and end-stage ☐ ☐
Maculopathy ☐ ☐

Take **blood glucose: if:**
Query Diabetic retinopathy (if subject reports no History) ☐
1 = Yes, 2 = No
Special (1:7 =40 years) ☐
Blood glucose (mmol/L) ☐☐.☐

Age-Related Macular Disease 1 = Yes 2 = No 9 = Not seen

ARM (drusen, hypo / hyper - pig. of RPE) ☐ ☐
ARMD a) dry / geographic atrophy ☐ ☐
b) wet / neovascular / disciform scar ☐ ☐

Other Vitreous / Retinal Pathology
1 = Yes, 2 = No 9 = No view ☐ ☐
Excluding diabetic retinopathy, Age-related macular degeneration
Details:

Digital Photos taken 1 = Yes, 2 = No ☐ ☐
(Red and Yellow cards)

Comments: ____

EXAMINERS INTIALS

MACHINE FAILURE ☐☐☐☐
1 = Autorefractometer, 2 = Slitlamp, 3 = VF, 4= Camera 5= U/S
SUBJECT FAILURE ☐☐☐☐
Subject refused 1=All tests 2=Dilation 3=Equipment

All Disorders that reduce vision in each eye
(Completed for all eyes ≤24 letters before refraction)

Principle cause of low vision or blindness in each eye
Mark only 1 cause per < 6/12 eye(s) (VA: =24 letters)

Principle cause of low vision or blindness in this subject (see note*)

Disorders	**R**	**L**	**R**	**L**	
Phthisical, disorganised or absent globe	☐	☐	☐	☐	☐
Refractive error	☐	☐	☐	☐	☐
Cataract	☐	☐	☐	☐	☐
Post Capsule opacification	☐	☐	☐	☐	☐
Uncorrected aphakia	☐	☐	☐	☐	☐
Corneal opacity* (Explain)	☐	☐	☐	☐	☐
Anterior uveitis	☐	☐	☐	☐	☐
Glaucoma* (Explain)	☐	☐	☐	☐	☐
Optic atrophy	☐	☐	☐	☐	☐
Diabetic retinopathy	☐	☐	☐	☐	☐
Other vascular retinopathy* (Explain)	☐	☐	☐	☐	☐
Chorioretinitis	☐	☐	☐	☐	☐
Macular degeneration	☐	☐	☐	☐	☐
Amblyopia (Refer to definition)	☐	☐	☐	☐	☐
Other / un-explained cause ____________	☐	☐	☐	☐	☐

* Details____

Underlying causes					
Unknown	☐	☐	☐	☐	☐
Trauma	☐	☐	☐	☐	☐
Congenital / Neonatal factor	☐	☐	☐	☐	☐
Measles/vitamin A deficiency/TEM	☐	☐	☐	☐	☐
Surgical procedure	☐	☐	☐	☐	☐
Onchocerciasis	☐	☐	☐	☐	☐
Trachoma	☐	☐	☐	☐	☐
Other, specify______________________	☐	☐	☐	☐	☐

Full diagnosis:

R eye: ____

L eye: ____

Current Action needed	**R eye**	**L eye**
• No current action needed	☐	☐
Action needed (tick all of which apply)		
• Eyelid surgery	☐	☐
• Cataract surgery	☐	☐
• Glaucoma treatment	☐	☐
• Spectacles	☐	☐
• Medication	☐	☐

- Other Action Right Eye ______________________________
- Other Action Left Eye_ ______________________________

Barriers to Up-take of Eye Care Services
(Indications: VA < 6/60; M-M cataract grades 2B or 3; TT grading)

Please rank numerically the first three res☐ses given by the subject.

Cannot afford	☐
No one to accompany	☐
No time	☐
Did not know about his / her eye disease	☐
Fear of treatment / surgery	☐
Waiting for cataract to mature	☐
Need not felt	☐
Does not know where to go for treatment	☐

Other ____

Candidate for Vision Function / Quality of Life questionnaire
(Indications: VA < 6/60 (<2 Letters); M-M cataract grades 2B or 3; 1 in every 20 Green cards)
TO THE INTERVIEWER ? ?

---

* Note: In cases of 'Cataract + Refractive Error', if the Best Corrected Visual Acuity is 6/18 or better (>18 letters), mark 'Refractive Error' as the cause. If not, mark 'Cataract'.

EXAMINERS INTIALS

☐

Appendix 3

Physicians' Practice Pattern for Glaucoma in Nigeria

Serial Number ☐☐☐ Zone ☐ State ☐☐ PIN ☐☐☐
FOR OFFICIAL USE ONLY Study code (zone/state/PIN x/xx/xxx) ☐☐☐☐☐☐

(Put an "x" for the appropriate response boxes and numbers where applicable) e.g. ☒ 1 9

1 Personal/Demographic details
(Please provide all details)

First Name ____________________ Surname ____________________
Sex Female ☐ Male ☐ Age (years) ☐☐

Address Hospital ____
Town ____________________
State ____________________

2 Professional Background

Ophthalmology qualification Fellowship ☐ Diplomate ☐ Other (specify) ☐ ______________
Number of years since ophthalmology qualification ☐☐

Are you a practising ophthalmologist? Yes ☐ No ☐
How many years have you been practising for? ☐☐

Have you had clinical subspecialty training? Yes ☐ No ☐
If yes, which subspecialty? ____________________
Number of years since subspecialty qualification ☐☐

Have you been practising as a subspecialist? Yes ☐ No ☐
Do you restrict your practice to your subspecialty? Yes ☐ No ☐

Do you participate in continuous professional development (CPD)/ continuous medical education (CME)? Yes ☐ No ☐

If yes,
Attendance at courses Yes ☐ No ☐ .---> Number of courses attended in the last 3 years ☐☐☐

Attendance at conferences Yes ☐ No ☐ .---> Number of conferences attended in the last 3 years ☐☐

Use of online CPD resources Yes ☐ No ☐ .---> If yes, name 2 top websites/programmes you use
1 ____________________ 2 ____________________

Use of journal CPD resources Yes ☐ No ☐ .---> If yes, name 3 journals that you regularly read
1 ______________ 2 ______________ 3 ______________

3 Place of practice

3.1 Type of facility (mark "x" in ALL that apply)

Government 1 ☐
Private 2 ☐
NGO/Missionary 3 ☐
Military 4 ☐

General hospital 1 ☐
General specialist hospital 2 ☐
Specialist eye hospital 3 ☐
University teaching hospital 4 ☐
Specialist eye teaching hospital 5 ☐
Other (specify) 6 ☐

Do you have **subspecialty clinics** in your hospital?
Yes ☐
No ☐

.----> If yes, which subspeciality clincis are taking place?
Glaucoma 1 ☐
Plastic and reconstructive surgery 2 ☐
Cornea and anterior segment 3 ☐
Vitreo-retina 4 ☐
Paediatric 5 ☐
Neuro-ophthalmology 6 ☐
Other (specify) ____________________ 7 ☐

Do you have visual rehabilitation services in your hospital?
Yes ☐
No ☐

.-----> If yes, tick the services available in your hospital
Patient counselling 1 ☐
Mobility training 2 ☐
Educational placement 3 ☐
Vocational placement 4 ☐
Other (specify) ____________________ 5 ☐

Do you have disease counselling services in your hospital?
Yes ☐
No ☐

3.2 Care-pathway (Mark "x" to all that apply)

How do patients access the services in your hospital?
Walk-in 1 ☐
Referral from other hospitals 2 ☐
Referral from community screening 3 ☐
Emergency 4 ☐
Other (specify) 5 ☐

How do patients specifically get to you as a Consultant?
First screened and selected by nurses 1 ☐
Screened and selected by optometrists 2 ☐
Seen and selected by residents 3 ☐
Seen directly by you 4 ☐
Other (specify) ____________________ 5 ☐

Is there a written/outlined protocol for management of glaucoma patients in your hospital?
Yes ☐
No ☐

3.3 Equipment

What equipment is available for your use for glaucoma diagnosis and treatment? (mark "x" to **ALL** that apply)

	Available in the hospital	Functioning	YOU use regularly
Ophthalmoscope	☐	☐	☐
Applanation tonometer	☐	☐	☐
Schiotz tonometer	☐	☐	☐
Other tonometer (specify) __________	☐	☐	☐
Gonioscope	☐	☐	☐
Slit-lamp with 60 - 90D lens	☐	☐	☐
Binocular indirect ophthalmoscope	☐	☐	☐
Visual field analyzer (specify type)	☐	☐	☐
____________________	☐	☐	☐
Fundus camera	☐	☐	☐
Ultrasound scan	☐	☐	☐
Optical coherent tomogram (OCT)	☐	☐	☐
Scanning laser ophthalmoscope (SLO)	☐	☐	☐
Laser machine for glaucoma treatment	☐	☐	☐
Other (specify) ____________	☐	☐	☐

4 Care for glaucoma

4.1 Diagnosis

On average, how many NEW glaucoma patients do you see in 3 months? ☐☐☐

What is the SINGLE most important feature that prompts you to work-up for glaucoma diagnosis? (mark "x" in **ONE** only)

- History ☐
- Visual Acuity ☐
- Visual field ☐
- Intra-ocular pressure ☐
- Disc morphology ☐
- AC angle morphology (gonio) ☐
- Corneal thickness ☐
- Colour vision defect ☐
- Night vision defect ☐
- Other (specify) ________________ ☐

Which of the following tests/examination do you ACTUALLY do on ALL your patients with glaucoma?

- Cup:Disc Ratio assessment Yes ☐ No ☐
- Gonioscopy Yes ☐ No ☐
- Optic nerve head imaging Yes ☐ No ☐
- Visual field examination Yes ☐ No ☐
- IOP measurement Yes ☐ No ☐
- Pachymetry Yes ☐ No ☐

When examining the disc to make a glaucoma diagnosis, if viewable, which of the following do you ACTUALLY use?

- Direct fundoscopy Yes ☐ No ☐
- Stereo-fundoscopy with +60/78/90D Yes ☐ No ☐
- Stereo-fundoscopy with contact lens Yes ☐ No ☐
- BIO with condensing lens Yes ☐ No ☐
- Fundus camera images Yes ☐ No ☐
- OCT Yes ☐ No ☐

4.2 Treatment

Most of our glaucoma patients present with late disease. Assuming all necessary equipment and treatment options are available and cost not a barrier, what is the best option of treatment that you WILL offer your glaucoma patient?

(mark x in **ONE** only)

- Medical (specify) ________________ 1 ☐
- Surgical (specify) ________________ 2 ☐
- Laser (specify) ________________ 3 ☐
- Observation and follow-up 4 ☐
- Other (specify) ________________ 5 ☐

What parameters do you use to make a choice of treatment?
(Mark "x" in all that apply)

- Severity of disease 1 ☐
- Availability of treatment 2 ☐
- Patient acceptance of treatment 3 ☐
- Cost of treatment 4 ☐
- Other (specify) ________________ 5 ☐

For the last 10 glaucoma cases you have seen:

- How many were offered surgery? ☐☐
- How many accepted surgery? ☐☐
- How many actually had surgery? ☐☐

4.3 Glaucoma Surgery

On average, how many glaucoma surgeries do you perform in 3 months? ☐☐☐

On average, how many cataract surgeries do you perform in 3 months? ☐☐☐

What type of glaucoma surgery do you most frequently perform? ________________________

Do you use anti-metabolites for glaucoma surgery?
Yes ☐
No ☐

Which antimetabolites do you use?
5 fluoro-uracil (5-FU) ☐
Mitomycin-C (MMC) ☐
Other (specify) ____________ ☐

If yes, for how many patients out of 10 would you use anti-metabolites? ☐☐

Where do you get the antimetabolites from?
The hospital's pharmacy ☐
Outside retail pharmacy ☐
Patients buy ☐
Doctor's supply by private arrangement ☐
Nurses supply by private arrangement ☐

Do you have any difficulties in obtaining a supply?
Yes ☐
No ☐

If yes, what are the difficulties?
____
____

What 3 main complications related to use of antimetabolites have you encountered in the last 10
1 ____________
2 ____________
3 ____________

Do you have an audit of outcome of surgery for the last 10 to 50 glaucoma surgeries you have performed?
Yes ☐
No ☐

5 Follow-up arrangement

Is there a written/outlined follow-up arrangement for glaucoma patients in your hospital?
Yes ☐
No ☐

How do you encourage/ensure follow-up?
You give an appointment date and hope the patient turns up ☐
No efforts are made to contact those who have missed their appointments ☐
Patient communication/reminders are sent
by email ☐
by phone ☐
by text ☐
by community/home visit ☐

Do you ask for the glaucoma patient to bring 1st degree relatives for examination?
All the time ☐
Some of the time ☐
Occassionally ☐
Never ☐

6 Costs

Do you know the costs of the different treatment options available for glaucoma?
Yes ☐
No ☐

What is the average cost of a course of medical therapy for one month? ____________ (Naira)

What is the cost of glaucoma surgery in your hospital, including standard hospital stay charges? ____________ (Naira)

What medications for glaucoma are available for you to prescribe? Mention all
____________ ____________
____________ ____________
____________ ____________
____________ ____________
____________ ____________
____________ ____________
____________ ____________

7 Challenges in glaucoma care

What are your perceived challenges in glaucoma care? (Mark "x" to ALL that apply)

- Fear of making a wrong diagnosis ☐
- Fear of surgical complications ☐
- Need for more training in glaucoma diagnosis ☐
- Need for more training in glaucoma surgery ☐
- Difficulty of post-op care ☐
- Uncertain post-op outcome ☐
- Patient compliance with medical treatment ☐
- Patient acceptance of surgical treatment ☐
- Other (specify) ____________________ ☐

How would you assess the training you received in glaucoma?

Excellent 1 ☐
Good 2 ☐
Fair 3 ☐
Poor 4 ☐
Very poor 5 ☐

Please write any additional comments in the box below

Thank you very much for taking time out to fill out this questionnaire

All respondents will be entered for a prize-draw Mark "x" if you do NOT want to be entered for the draw ☐

Appendix 4a

Information Sheet – Physicians practice pattern

Greetings

Principal investigator and researchers

I am Fatima Kyari, an ophthalmologist working on a research project at the London School of Hygiene and Tropical Medicine (LSHTM), under the supervision of Professor Clare Gilbert. Working together with research assistants and fieldworkers, we are looking for more information on glaucoma.

The research is funded by Fred Hollows Foundation, an independent, non-profit, politically unaligned and secular NGO involved in eye care.

Ethical permission

We have obtained ethical permission to conduct this study from the LSHTM and the Federal Ministry of Health.

Background

Accounting for 12% of world blindness (excluding refractive errors), glaucoma is the second leading cause of blindness (Resnikoff, 2004). It is projected that glaucoma will affect 60 million people worldwide by 2010, of which 45 million will have OAG, with the highest percentage of 4.16% of 40 year-olds and older in Africa (Quigley and Broman, 2006). The Nigerian national survey of blindness and low vision (NBS), which included 13,500 people aged 40 years and above showed the prevalence of blindness to be 4.2%. Glaucoma was the second leading cause (16.3%) with over 180,000 Nigerians being blind from glaucoma (Kyari et al, 2009).

Interventions to prevent blindness from glaucoma aim at lowering IOP and include surgical (mostly trabeculectomy), laser and medical therapies. While highlighting acceptable surgical outcomes for trabeculectomy in Africa, difficulties and challenges of glaucoma management in west Africa have been documented (Egbert, 2002). The cost of glaucoma medication and the economic burden of disease in the United States have been demonstrated using the life-table model (Quigley, 2005).

Study objectives and relevance

We want to find out how glaucoma is currently being managed in Nigeria; in terms of service delivery to patients; what glaucoma treatment is available and how much they cost. We seek your cooperation because the information is relevant for hospitals and government to improve the quality and extent of services provided in order to prevent the glaucoma patient from losing vision.

Participation

You are asked to take part in the study because you are an ophthalmologist providing eye care services. It is voluntary for you to participate. If you agree to participate, we will ask you to complete a questionnaire, which will take about 15 minutes. The questions are about your pattern of practice for eye care, infrastructure and equipment available to you for glaucoma care and information on the types of glaucoma patients you see. If you agree to participate now, you still have the right to withdraw at anytime.

Confidentiality and use of the data

The information obtained will not be linked to you (anonymity) and all data will be kept secured and used only by those involved in the study. No quotes or other results arising from your participation in this study will be included in any reports, even anonymously, without your agreement. The analysed results will be disseminated to World Health Organization, government, health care workers and through publications.

Consent

If you have agreed to participate please complete and sign the questionnaire attached.

Thank you for your time and for the information.

Further information

Should you have any questions after we leave, or you seek further information or explanation, please contact Fatima Kyari at the address below.

Dr Fatima Kyari
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Email: Fatima.Kyari@lshtm.ac.uk
fatimaygk@gmail.com

Appendix 4b

Information Sheet – Community Perception - Interviews

This will be read out to potential participants. A translated version in the local language will also be used.

Greetings

Principal investigator and researchers

I am Fatima Kyari, an eye doctor and I am working on a research project with staff at the London School of Hygiene and Tropical Medicine (LSHTM), under the supervision of Professor Clare Gilbert. We are aware that eye conditions are quite common in the community and we want to find out what community members know about conditions of the eye so that services for eye conditions can be better planned.

The research is funded by Fred Hollows Foundation, an independent, non-profit, politically unaligned and secular NGO involved in eye care.

Ethical permission

We have obtained ethical permission to conduct this study from the LSHTM and the Federal Ministry of Health.

Background

The Nigerian national survey on blindness and low vision conducted in 2005 to 2007 showed that some eye conditions are important causes of poor vision in our communities.

Study objective and relevance

We want to find out what you know, think and do about some eye diseases. In particular we want to find out what you know about a condition called glaucoma. We want to find out if you know what treatment is possible, and how much money is spent on treating it. We seek your cooperation because the information is relevant for clinics, hospitals and government to improve the quality and extent of services provided.

Participation

You are asked to take part in the study because your community was selected for the study and you have visual impairment. It is voluntary for you to participate. If you agree to participate, we will interview you for 10 to 15 minutes. The interview will be in a private room and it will be recorded and transcribed to aid our analysis. Photographs will also be taken which may be used for publication or electronically in a manner of which you may or may not be identified. However, you may decide not to participate in the interview or not agree to be recorded or have your photo taken. And if you agree now, you still have the right to withdraw at anytime during the interview.

Confidentiality and use of the data

The interview will not affect any treatment you are receiving for any health condition that you may have. But if we feel there is a need to improve the treatment or address other health issues, we will indicate that. We will also give you a referral to the hospital and take the necessary steps to make sure you receive the necessary services.

The information obtained will not be linked to you (anonymity) and all data will be kept secured and used only by those involved in the study. No quotes or other results arising from your participation in this study will be included in any reports, even anonymously, without your agreement. The analysed results will be disseminated to World Health Organization, government, health care workers and through publications.

Consent

If you have agreed to participate please read (*or will be read*) and sign (*or thumb print*) the consent form attached.

Thank you for your time and for the information.

Further information

Should you have any questions after we leave, or you seek further information or explanation, please contact Fatima Kyari at the address below.

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Email: Fatima.Kyari@lshtm.ac.uk

Appendix 4c

Information Sheet – Community Perception – Observation studies

This will be read out to potential participants. A translated version in the local language will also be used.

Greetings

Principal investigator and researchers

I am Fatima Kyari, an eye doctor and I am working on a research project with staff at the London School of Hygiene and Tropical Medicine (LSHTM), under the supervision of Professor Clare Gilbert. We are aware that eye conditions are quite common in the community and we want to find out what community members know about conditions of the eye so that services for eye conditions can be better planned.

The research is funded by Fred Hollows Foundation, an independent, non-profit, politically unaligned and secular NGO involved in eye care.

Ethical permission

We have obtained ethical permission to conduct this study from the LSHTM and the Federal Ministry of Health.

Background

The Nigerian national survey on blindness and low vision conducted in 2005 to 2007 showed that some eye conditions are important causes of poor vision in our communities.

Study objective and relevance

We want to find out how you are coping with your eye condition and how it affects your day-to-day living. We also want to find out what you know about a condition called glaucoma. We want to find out if you have it; if you know what treatment is possible, and how much money you spend on treating it. We seek your cooperation because the information is relevant for clinics, hospitals and government to improve the quality and extent of services provided.

Participation

You are asked to take part in the study because your community was selected for the study and you have been identified to have poor eye sight. It is voluntary for you to participate. If you agree to participate, we will spend 3 to 6 hours with you while you carry out your normal day-to-day activities. We will also interview you. The interview will be recorded and transcribed to aid our analysis. Photographs will also be taken which may be used for publication or electronically in a manner of which you may or may not be identified. However, you may decide not to participate in the interview or not agree to be recorded or have your photo taken or to be observed. And if you agree now, you still have the right to withdraw at anytime during the interview/observation.

Confidentiality and use of the data

The discussions will not affect any treatment you are receiving for any health condition that you may have. But if we feel there is a need to improve the treatment or address other health issues, we will indicate that and give you a referral to the hospital and take the necessary steps to make sure you receive the necessary services.

The information obtained will not be linked to you (anonymity) and all data will be kept secured and used only by those involved in the study. No quotes or other results arising from your participation in this study will be included in any reports, even anonymously, without your agreement. The analysed results will be disseminated to World Health Organization, government, health care workers and through publications.

Consent

If you have agreed to participate please read (*or will be read*) and sign (*or thumb print*) the consent form attached.

Thank you for your time and for the information.

Further information

Should you have any questions after we leave, or you seek further information or explanation, please contact Fatima Kyari at the address below.

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Appendix 4d

Information Sheet – Patient Perception

This will be read out to potential participants. A translated version in the local language will also be used.

Greetings

Principal investigator and researchers

I am Fatima Kyari, an eye doctor working on a research project with staff at the London School of Hygiene and Tropical Medicine (LSHTM), under the supervision of Professor Clare Gilbert. Working together with research assistants and fieldworkers, we are looking for more information on eye conditions and what you may know about them.

The research is funded by Fred Hollows Foundation, an independent, non-profit, politically unaligned and secular NGO involved in eye care.

Ethical permission

We have obtained ethical permission to conduct this study from the LSHTM and the Federal Ministry of Health.

Background

The Nigerian national survey on blindness and low vision conducted in 2005 to 2007 showed that some eye conditions are important causes of poor vision in our communities.

Study objectives and relevance

We want to find out what you know, think and do about some eye diseases. In particular we want to find out what you know about your condition called glaucoma. We want to find what you know about treatment of the condition and how much money you spend on treating it. We seek your cooperation because the information is relevant for clinics, hospitals and government to improve the quality and extent of services provided.

Participation

You are asked to take part in the study because you are a glaucoma patient receiving treatment in the hospital. It is voluntary for you to participate. If you agree to participate, we will be interviewed for 10 to 15 minutes. The interview will be in a private room and it will be recorded and transcribed to aid our analysis. Photographs will also be taken which may be used for publication or electronically in a manner of which you may or may not be identified. However, you may decide not to participate in the interview or not agree to be recorded or have your photo taken. And if you agree now, you still have the right to withdraw at anytime during the interview.

Confidentiality and use of the data

The interview will not affect your current treatment in the hospital but if we feel there is a need to improve the treatment or address other health issues, we will indicate that to your attending physician.

The information obtained will not be linked to you (anonymity) and all data will be kept secured and used only by those involved in the study. No quotes or other results arising from your participation in this study will be included in any reports, even anonymously, without your agreement. The analysed results will be disseminated to World Health Organization, government, health care workers and through publications.

Consent

If you have agreed to participate please read (*or will be read*) and sign (*or thumb print*) the consent form attached.

Thank you for your time and for the information.

Further information

Should you have any questions after we leave, or you seek further information or explanation, please contact Fatima Kyari at the address below.

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Appendix 5

Informed Consent Form

Glaucoma in Nigeria:
A study about glaucoma treatment and service delivery; and patients and community perception of the condition

Investigator's name and contact details

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To be completed by participant (Please tick as appropriate)

		Yes	**No**
1	I have read the information sheet concerning this study (or have understood the verbal explanation), and I understand what is required of me and what will happen to me if I take part		
2	My questions concerning this study have been answered by the researchers		
3	I understand that at anytime I may decide not to participate without giving any reason.		
4	I agree that you record what we talk about		
5	*I agree that you take photos during our discussions for the study		
6	*I agree that you use quotes of things I say in the discussions in any reports about the study		
7	*I agree that you use quotes of things I say in the discussions **only** anonymously, in any reports about the study.		
8	I agree that results arising from my participation in the study can be included in any reports about the study		
9	I agree that any discussions and results arising from any general analyses (rather than individual quotes) that deal with the data can be included in any reports about the study		
10	I agree to take part in the study		

*Participants may decide not agree for their photos to be taken and use of quotes.
All other fields must be agreed by the participant in order to take part in the study.

Participant (name in BLOCK LETTERS) ______________________________

Signed ______________________________

Date ____________

Witness (name in BLOCK LETTERS) ______________________________

Signed ______________________________

Date ____________

Strengthening Institutional Capacity for Glaucoma Care in Sub-Saharan Africa

Karim F. Damji

‘An enabling environment’ -A setting in which additional development initiatives can take root and thrive.

His Highness the Aga Khan, Maputo, Mozambique, December 16, 2010.[1]

Sub-Saharan Africa (SSA) is advancing economically, and these are exciting times to invest in improvement of vision related quality of life for the people in this region.[2] In SSA, a leading cause of blindness is glaucoma, a group of diseases that have in common a characteristic progressive optic neuropathy and visual field deterioration, which can generally be arrested or mitigated with lowering of intraocular pressure (IOP). Glaucoma is a disease with a significant public health burden that warrants a commensurate, targeted response. This is a conclusion emphasized at two major meetings on the subject in recent years: The Africa Glaucoma Summit in Accra, Ghana hosted by the World Glaucoma Association (August 2010)[3] and a Workshop on Public Health Control of Vision Loss from Glaucoma in Africa hosted by the Prevention of Blindness Union in collaboration with International Agency for the Prevention of Blindness Africa in Kampala, Uganda (April 2012).[4] This clarion call is also evident when we examine the data presented by Kyari *et al*.[5] in their outstanding article, which leads this theme issue “Glaucoma in SSA”. A challenging picture of glaucoma emerges from the above sources:

- Glaucoma is the second leading cause of blindness worldwide with Africa disproportionately affected.
- There are an estimated 6 million people with potentially blinding or disabling glaucoma in Africa while 0.5 million are already blind from the disease.
- The estimated prevalence of glaucoma is approximately 4% among people 40 years and older. This figure is likely an underestimate as it is often difficult to diagnose glaucoma when there is coexistent media opacity such as cataract/corneal opacity, and many studies to date do not include visual field data as part of the diagnosis.
- The most common form of glaucoma is primary open angle glaucoma, which is approximately six times more common than angle closure; however, there is a paucity of good epidemiological data, particularly with regard to other types of glaucoma such as exfoliation related glaucoma.
- The awareness of glaucoma is very low, and a large majority of patients are untreated. In fact, 90% or more of those with glaucoma remain undiagnosed. The article by Komolafe *et al*.[6] examines the level of awareness amongst non-ophthalmic health-care personnel and how these individuals can be empowered to play a more active role in raising patient awareness. The articles on “teleglaucoma” by Kassam *et al*.[7] and Kiage *et al*.[8] propose a creative response, that needs to be studied further, to promote access based on the provision of expert care from a distance.
- When patients do present, at least half do so with advanced disease and of these, over half are blind in one eye. The article by Josephine *et al*.[9] reports on important barriers to glaucoma surgery in Nigeria including fear of blindness. The article on advanced glaucoma by Gessesse and Damji[10] provides practical tips for managing these challenging patients, including, approaching patients through an integrated “biopsychosociospiritual” frame-work, and pearls to optimize trabeculectomy technique so as to protect vision and prevent/minimize chances of visual field “wipe out.”
- Risk factors for developing open-angle glaucoma in SSA include increasing age, higher IOP, lower systolic blood pressure (BP) to IOP ratio (BP/IOP), lower mean diastolic ocular perfusion pressure (diastolic BP minus IOP), thinner central corneal thickness, and a positive family history of glaucoma. Can future programs aimed at detecting glaucoma leverage these and any other high risk characteristics?
- There is much that needs to be studied in order to arrive at better ways of managing glaucomas in various SSA contexts. One technique that may be of value in challenging cases is an aqueous drainage device, and the article by Aminlari *et al*.[11] offers insight in this regard.

There are many barriers, which prevent patients from receiving appropriate care including geographic, educational,

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socioeconomic, cultural/spiritual, and political considerations, as well as lack of adequate facilities, human resources, equipment, medication, laser, and surgical treatment options. Although, this is a daunting list, progress is being made in terms of acknowledging the magnitude and importance of the problem and taking steps toward addressing these challenges. Recently, a very practical guide to diagnosis and management of glaucoma in the SSA context was published, and I would recommend all involved with such efforts to read the special issue of the Community Eye Health Journal Vol. 25 Issues 79 and 80, 2012.[12] The value of eliminating avoidable blindness and visual impairment in developing countries is underscored in a recent report by price water house Coopers commissioned by The Fred Hollows Foundation and other key non-governmental organizations. Using a conservative estimate, they illustrate that for every dollar invested in preventing someone from going blind, more than four dollars in economic benefits are generated.[13] This estimate does not factor in further gains to quality of life that accrue from improved vision health.

An important question to ask is what can be carried out to strengthen detection and management of glaucoma at the primary, secondary and tertiary levels? Building solid tertiary institutional capacity can provide a hub for integration of primary, secondary and tertiary approaches to glaucoma care. Outstanding institutions, networked with other like-minded and like-hearted Institutions and eye care partners, can catalyze and propel advances in patient centered care, education, research, and health-care policy. Whether or not an institution achieves excellence and success in these endeavors is predicated on solid leadership and governance that nurtures a culture of respect, continuous learning and collaboration, as well as excellence in clinical, educational and research environments.

LEADERSHIP AND GOVERNANCE

The quality of institutions is directly dependent on the quality of leadership that is provided, nurtured, and sustained and how this leadership utilizes the institutional framework to deliver its services. This includes setting international standards of care and effectively leading a team of eye care professionals such as ophthalmologists, nurses, optometrists, pharmacists, and counselors. Creating a learning organization that continuously transforms itself is also a key to success.[14] In my view, greater thought is required so that over the next 5 years, programs and processes are in place to ensure a continuous pipeline of physicians as well as other leadership talent is being developed that will serve SSA in the short term and for the long term in a sustainable manner.

Leadership in institutions is exercised through good governance, i.e., how an organization can utilize structure and process to exercise power effectively. Good governance includes the following elements: Clear structure and organization, an understanding of vision, mandate, and responsibilities, an organizational culture that promotes continuous learning and collaboration, transparency and probity as well as team spirit and high performance, robust processes and information, and performance assessment and accountability. The quality of various institutional processes as well the physical environment (i.e., the spaces in which one works and learns) will be critical to ensuring high quality clinical outcomes and patient satisfaction, which ultimately form part of the raison d'être for service institutions.[15]

INSTITUTIONAL MODELS, SUSTAINABLE HUMAN, FINANCIAL AND INFORMATION TECHNOLOGY RESOURCES AND IMPORTANCE OF MEASURING RESULTS

There are many models of eye care institutions in SSA. These include public, private, civil society, as well as emerging models of social entrepreneurship and public private partnership. These institutions also need to be viewed in the context of health care systems. Hence, consideration thus needs to be given to pragmatic issues such ensuring a stable supply chain of medications and equipment.[15] Structuring institutions for long term success will also require optimal utilization of finite human, financial, and information technology related resources. Developing strong professional managers who can lead various operations teams (clinical, operating, biomedical engineering, community outreach etc.) is a key ingredient in this regard.[16] On the financial front, sustainable sources of income are required, developing high efficiency, appropriate budget and price for various services, and effective cost-control measures.[16] Standard protocols, processes for continuous improvement, monitoring and empowering staff, and succession planning are methods by which the other dimensions of sustainability can be addressed.[16] Developing key metrics to track efficiency and effectiveness as well as a culture of accountability is also key to achieving excellence in institutional performance. The balanced scorecard is one approach, which can provide a framework for developing and tracking key performance measures, including in developing national academic hospitals.[17,18]

TEACHING AND LEARNING ENVIRONMENT AND MULTIPLIER EFFECT

Developing an outstanding teaching and learning environment is essential to developing outstanding human resources. These individuals can then have a powerful ripple or multiplier effect, empowering various members of the eye care team, as well as student learners with knowledge and skills to detect and manage glaucoma at various levels. Over the past 6 years, I have been fortunate to work with several tertiary care institutions in Kenya and Ethiopia in order to assist in institutional capacity development utilizing the "sandwich" educational model.[19] The essence of this model has been to gradually strengthen institutional capacity through international standard subspecialty training while simultaneously enhancing the patient care, teaching/learning and research environments. The model helps provide an "enabling environment" for professional growth, which we hope fosters retention of individuals and provides a gateway into long term, mutually beneficial collaborative partnerships.

"Sandwich" fellowship graduates to date have been successful in helping to modify curricula for residency training, improve standards of care for patients with glaucoma, and develop models for raising awareness of glaucoma in communities. They have also helped in detecting/managing earlier stages of disease, including via creative "teleglaucoma" approaches, as well as contributing to the development of national guidelines for glaucoma, such as those being developed in Kenya (personal communication Drs. Dan Kiage and Sheila Marco).

RESEARCH AND KNOWLEDGE TRANSLATION

A number of centers in SSA are now well positioned to conduct research at various levels, i.e., population, clinical, and basic science as well as a partner with other regional and international institutions/entities. Conducting and publishing high-quality research will not only lead to a better understanding of how to advance patient care specific to SSA, but can also uplift the educational environment attracting bright minds and entrepreneurial investment long-term. Several interesting questions need to be addressed (the Kampala workshop[4] and the Kyari article[5] contains some excellent ideas in this regard):

- What is the prevalence of various types of glaucoma types in the various countries and subpopulations? Are subtypes such as neovascular glaucoma on the rise given the rapid increase in the prevalence of diabetes and if so, what steps can be taken to mitigate this trend?
- What is the level of awareness of glaucoma, what are barriers to awareness, and what can be carried out to improve the level of awareness?
- What are the specific barriers in SSA for access to glaucoma care, as well as for compliance and adherence to treatment and how can these be overcome?
- How can glaucoma best be detected and managed? Randomized controlled trials are needed, cost and comparative effectiveness studies, quality of life studies. Program level research is needed so as to learn from pilot studies and then replicate and scale up successful projects.
- What are underlying genetic and environmental factors that play a role in the pathogenesis of various glaucomas in SSA?
- Clinical guidelines are needed to offer best practice and thinking on detection of various glaucomas, identification of the stage of disease, and appropriate medical, laser, and surgical management options. Guidelines also need to consider treatment options for absolute glaucoma (a blind eye, which is often painful as well) and for vision rehabilitation/support.
- What tools and metrics can be utilized to monitor and study the impact of various activities/interventions on vision related quality of life?
- Health systems research is also required that includes the development of innovative health delivery models, in particular to be able to provide glaucoma care to those who are unable to afford it.

RELEVANCE TO ENHANCING GLAUCOMA CARE

Glaucoma is an enormous problem in SSA and given the demographic trends, will be an even greater challenge in the decades ahead. Hence, it is essential that glaucoma be widely recognized as a serious public health concern and creative steps taken to eliminate avoidable blindness from this group of diseases. One of the key steps, in my view, is to strengthen institutional capacity for glaucoma care. A year ago I had proposed the idea of a special issue of MEAJO dedicated to glaucoma in SSA in order to better inform readers of the current landscape and encourage a call to action for the benefit of current and future generations in SSA. I am very pleased that this issue has now reached fruition and I would like to thank the editors of the journal for the privilege of having served as guest editor and for the opportunity to write this editorial. I would also like to thank all peer reviewers for their enormous contribution of knowledge, time and energy.

I hope that over the next decade, we are able to build solid capacity for integrated glaucoma care at the primary, secondary and tertiary levels in SSA and that glaucoma centers of excellence can partner with and continue to learn from the best that local and global stakeholders have to offer so that they can advance to better serve their patients and communities. This will necessitate continued development of a new generation of subspecialists with leadership/management skills that can entrench good governance and develop other members of the eye care team, partnerships with a variety of public and civil society players, and the creation of enabling environments for patient care, education and research where "new initiatives can take root and thrive" and patients with or at risk for glaucoma receive international standard care to protect visual function and maintain or enhance their overall health related quality of life.

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Thank you for your contribution to our journal.
With personal regards
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Appendix 7b

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Best regards,

Joanne

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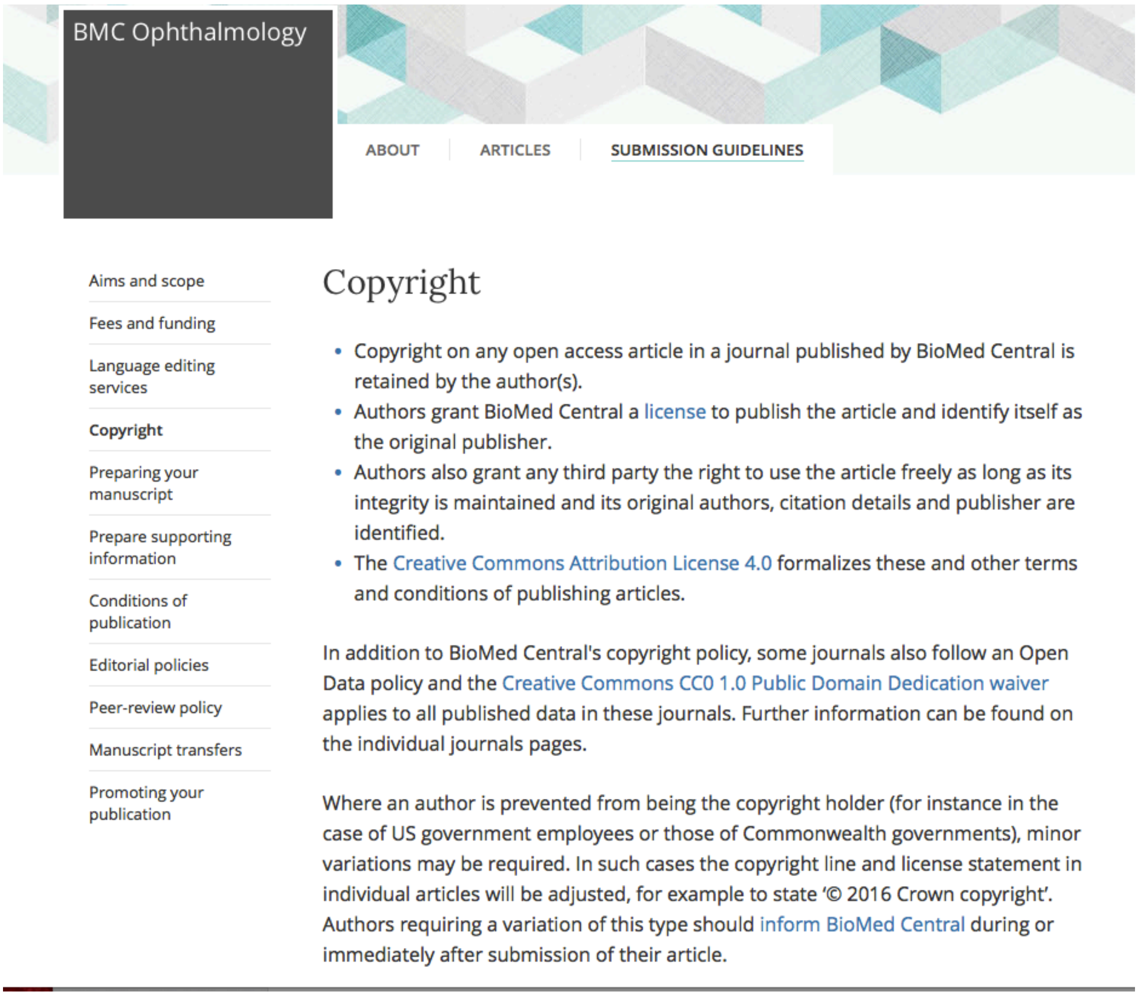
Appendix 7c



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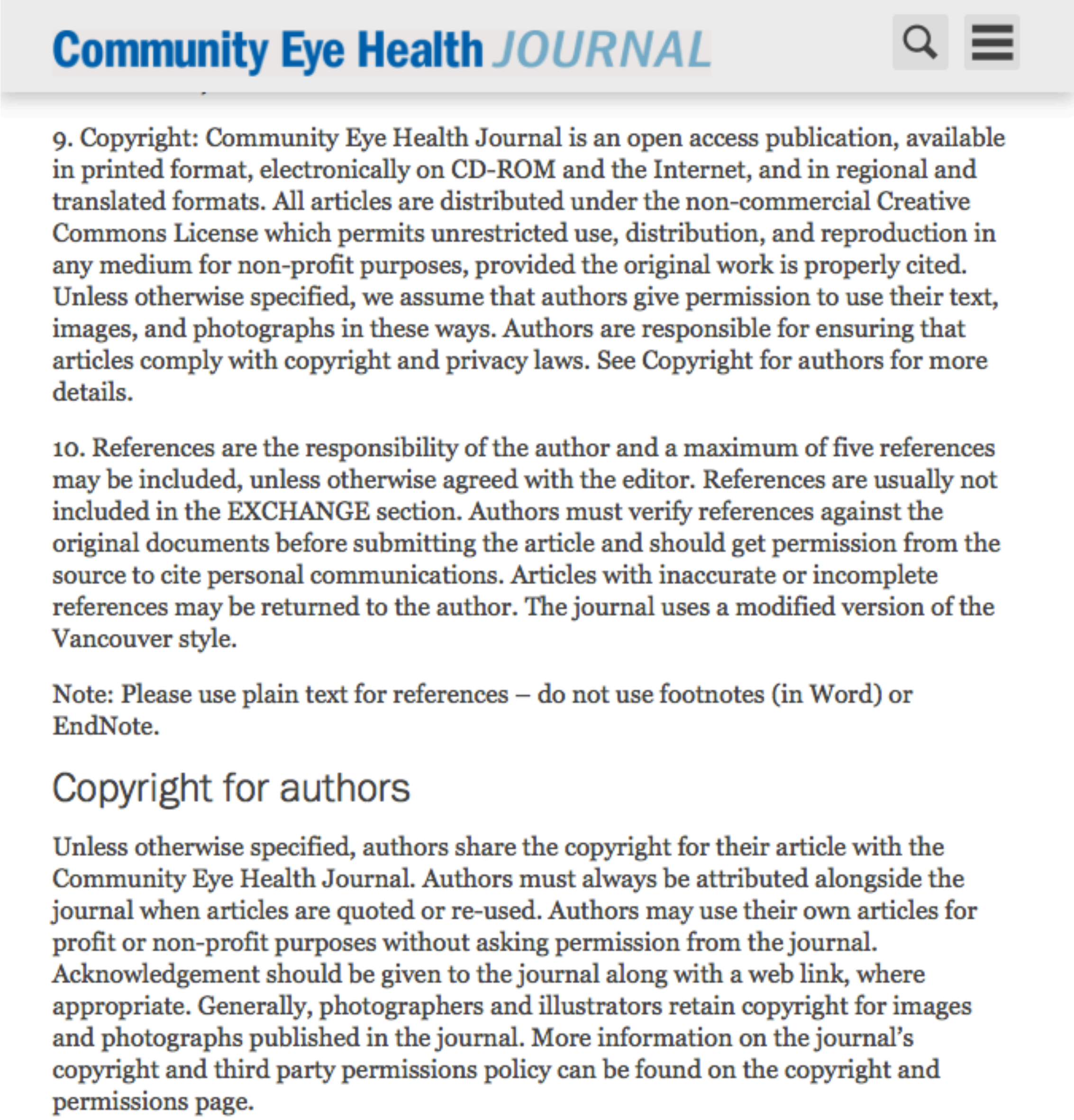

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Appendix 8a

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled "Evidence for improving services for glaucoma in Nigeria."

1. Kyari F, Abdull MM, Wormald R, Evans JE, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. Risk factors for open-angle glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2016; 16:78. DOI 10.1186/s12886-016-0264-7.
2. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.
3. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.
4. Kyari F, Abdull MM, Bastawrous A, Gilbert CE, Faal H. Epidemiology of glaucoma in sub-saharan Africa: prevalence, incidence and risk factors. Middle East Afr J Ophthalmol. 2013 Apr-Jun;20(2):111-25. doi: 10.4103/0974-9233.110605. Review. PubMed PMID: 23741130; PubMed Central PMCID: PMC3669488.

Name: Clare Gilbert

Sign:

Date: July 31 2016

Appendix 8b

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled "Evidence for improving services for glaucoma in Nigeria."

1. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.

2. Kyari F, Abdull MM, Bastawrous A, Gilbert CE, Faal H. Epidemiology of glaucoma in sub-saharan Africa: prevalence, incidence and risk factors. Middle East Afr J Ophthalmol. 2013 Apr-Jun;20(2):111-25. doi: 10.4103/0974-9233.110605. Review. PubMed PMID: 23741130; PubMed Central PMCID: PMC3669488.

Name: Hannah Faal

Sign: Faal

Date: July 30th 2016

Appendix 8c

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled "Evidence for improving services for glaucoma in Nigeria."

1. Kyari F, Abdull MM, Wormald R, Evans JE, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. Risk factors for open-angle glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2016; 16:78. DOI 10.1186/s12886-016-0264-7.
2. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.
3. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.

Name: Richard Wormald

Sign: signed electronically by Richard

Date: 1st August 2016

Appendix 8d

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Abdull MM, Wormald R, Evans JE, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. Risk factors for open-angle glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2016; 16:78. DOI 10.1186/s12886-016-0264-7.
2. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.

Name: Winifred Nolan

Sign:

Date: 3/8/2016

Appendix 8e

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.
2. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.

Name: Paul Spry

Sign:

Date:01/08/2016

Appendix 8f

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Abdull MM, Wormald R, Evans JE, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. Risk factors for open-angle glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2016; 16:78. DOI 10.1186/s12886-016-0264-7*.*
2. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.

Name: Gudlavalleti VS Murthy

Sign: G.V.

Date: 1st August 2016

Appendix 8g

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.

Name: Mansur Rabiu

Sign:

Date: 4 Aug, 2016

Appendix 8h

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Abdull MM, Wormald R, Evans JE, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. Risk factors for open-angle glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2016; 16:78. DOI 10.1186/s12886-016-0264-7.
2. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.
3. Kyari F, Abdull MM, Bastawrous A, Gilbert CE, Faal H. Epidemiology of glaucoma in sub-saharan Africa: prevalence, incidence and risk factors. Middle East Afr J Ophthalmol. 2013 Apr-Jun;20(2):111-25. doi: 10.4103/0974-9233.110605. Review. PubMed PMID: 23741130; PubMed Central PMCID: PMC3669488.
4. Kyari F, Abdull MM. Managing a patient with open-angle glaucoma: a case study. Community Eye Health. 2012;25(79-80):71-2. PubMed PMID: 23520424; PubMed Central PMCID: PMC3588137.

Name: Mohammed M. Abdull

Sign: AbdullMM

Date: 30 July 2016

Appendix 8i

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled "Evidence for improving services for glaucoma in Nigeria."

1. Kyari F, Entekume G, Rabiu M, Spry P, Wormald R, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. A Population-based survey for the prevalence and types of glaucoma in Nigeria. The Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2015;15:176. doi:10.1186/s12886-015-0160-6.

Name: Gabriel Entekume
Sign:
Date: 4TH August, 2016.

Appendix 8j

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled "Evidence for improving services for glaucoma in Nigeria."

1. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.

Name: Tunde Peto

Sign:

Date: 2nd August 2016.

Appendix 8k

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled "Evidence for improving services for glaucoma in Nigeria."

1. Kyari F, Abdull MM, Sallo FB, Spry PG, Wormald R, Peto T, Faal HB, Gilbert CE; Nigeria National Blindness and Visual Impairment Study Group. Nigeria normative data for defining glaucoma in prevalence surveys. Ophthalmic Epidemiol. 2015 Apr;22(2):98-108. doi: 10.3109/09286586.2015.1012268. PubMed PMID: 25777309.

Date: July 30, 2016.

Sign: Dr Sallo

Name: Ferenc B. Sallo

Appendix 8l

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Abdull MM, Wormald R, Evans JE, Nolan W, Murthy GVS, Gilbert CE, on behalf of the Nigeria National Blindness and Visual Impairment Study Group. Risk factors for open-angle glaucoma in Nigeria. Results from the Nigeria National Blindness and Visual Impairment Survey. BMC Ophthalmology. 2016; 16:78. DOI 10.1186/s12886-016-0264-7.

Name: Jennifer E. Evans

Sign: Jennifer Evans

Date: 1/8/2106

Appendix 8m

To Fatima

I agree that our work indicated below can be included in its/their published format in your thesis titled “Evidence for improving services for glaucoma in Nigeria.”

1. Kyari F, Abdull MM, Bastawrous A, Gilbert CE, Faal H. Epidemiology of glaucoma in sub-saharan Africa: prevalence, incidence and risk factors. Middle East Afr J Ophthalmol. 2013 Apr-Jun;20(2):111-25. doi: 10.4103/0974-9233.110605. Review. PubMed PMID: 23741130; PubMed Central PMCID: PMC3669488.

Name: Andrew Bastawrous

Sign: A.Bastawrous

Date: 30/07/16